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ORIGINAL ARTICLE

The impact of chronic myeloid leukemia on employment: the French prospective study

Sandra De Barros[1] · Flora Vayr[2] · Fabien Despas[1,3,4] · Mathilde Strumia[1] · Clémentine Podevin[1] · Martin Gauthier[5] · Eric Delabesse[6] · Jean-Marc Soulat[2,4] · Guy Laurent[4,5] · Françoise Huguet[5] · Fabrice Herin[2,4]

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Abstract

Patients with chronic myeloid leukemia treated with breakpoint cluster region-Abelson tyrosine kinase inhibitors are likely to survive in excess of 20 years after diagnosis. New challenges appear as we consider life after the disease, including professional challenges and the social reintegration of patients. The purpose of this study was to determine the impact of chronic myeloid leukemia on employment within 2 years after diagnosis. This prospective, observational study included patients diagnosed with chronic myeloid leukemia and treated with a tyrosine kinase inhibitor. Two populations were defined as patients who reported modifications in their professional activity during the study (Acti-Pro+) and patients who did not report a modification (Acti-Pro−). Cancer survivors received a self-assessment questionnaire. The primary endpoint was to determine the professional status of patients. One hundred patients completed the questionnaire. Sixty-six patients out of 100 reported professional activity within 2 years after their diagnosis. During the 2 years after the diagnosis, 65.2% (95% confidence interval (CI), 53.7–76.7) of patients faced modifications in their professional activity due to chronic myeloid leukemia or adverse effects of drug treatments (group Acti-Pro+); in contrast, 34.8% of patients did not report any impact on their occupational activity (group Acti-Pro−). Among modifications to work organization, a change in the number of working hours was the most represented. Other modifications comprised changes in status or work pace. A majority of chronic myeloid leukemia patients face professional consequences of their disease and treatments. Our findings suggest that adverse drug reactions are a major factor affecting the occurrence of work modifications in this context.

Keywords Cancer · Chronic myeloid leukemia · Return to work · Occupational health practice

Sandra De Barros and Flora Vayr contributed equally to this work.

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✉ Fabrice Herin
herin.f@chu-toulouse.fr

[1] Department of Clinical Pharmacology, Toulouse University Hospital, Toulouse, France

[2] Department of Occupational Diseases, Toulouse University Hospital, Bâtiment Turiaf, Place du Dr Baylac, 31059 Toulouse Cedex 9, France

[3] Laboratory of Clinical Pharmacology, Université Toulouse III, Toulouse, France

[4] INSERM UMR1027 (The French National Institute of Health and Medical Research), Université Toulouse III, Toulouse, France

[5] Department of Hematology, Toulouse University Hospital, IUCT-O, Toulouse, France

[6] Hematology Laboratory, Toulouse University Hospital, Toulouse, France

Background

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm of hematopoietic stem cells affecting mostly adults. CML results from a translocation between chromosomes 9 and 22 leading to the collocation of the *breakpoint cluster region* (*BCR*) protein and *Abelson murine leukemia viral oncogene homolog 1* (*ABL*) genes. This causes the fusion of a *BCR-ABL* gene encoding for the synthesis of a BCR-ABL protein including tyrosine kinase activity and responsible for phosphorylation of several substrates which activate multiple signal-transduction cascades involved in cell proliferation and differentiation. The worldwide incidence rate of the disease is 1.0 per 100,000 for men and 0.6 per 100,000 for women [1]. CML is characterized by an initial chronic phase followed by the progression to accelerated and blastic phases, the latter always leading to patient death. The average lifespan ranged from 5 to 10 years before the development of innovative molecular therapies which target newly formed protein with

tyrosine kinase activity [2]. BCR-ABL tyrosine kinase inhibitors (TKIs) are now systematically prescribed to every patient presenting with chronic phase CML. In the case of a response to a TKI, they are likely to survive in excess of 20 years after diagnosis [3], with 10-year survival rates currently reaching 84%. As patients have increased expected lifespan, new challenges appear. These include evaluating quality of life or the costs of the aforementioned new treatments. Studies have focused on describing the quality of life of patients [4–6], but often omitting to consider its social and professional dimensions. The ability to perform an occupational activity contributes to the improvement of quality of life [7], although few studies have been actively focused on the professional impact of CML. A Danish study reported that patients with CML are 14 times more likely to receive daily disability pension 2 years after diagnosis compared to the general population [8]. The purpose of this study was to determine the impact of CML on employment within 2 years after diagnosis. We describe the medical characteristics of patients and self-reported quality of life measures, considering both social and professional integration. Finally, we report practical arrangements and changes in work organization necessary for these patients to return to work.

Methods

This prospective, observational study was carried out at Toulouse University Hospital. The patients were men and women over the age of 18 years with CML diagnosed between 1 January 2009 and 31 December 2014, treated with a TKI. They were covered by French national health insurance, and they were not subject to any legal protective measures. Patients failing to meet these criteria, refusing to participate, or with general comprehension difficulties were not included. Patients were identified using data generated by the cytogenetic and molecular biology laboratory of hemopathies of Toulouse University Hospital (IUCT-O). Two databases were used and cross-referenced to gather the maximum data possible. The inclusion criteria were those with suspicions of CML associated with a translocation t(9;22) and patients with a positive polymerase chain reaction (PCR) for the *BCR-ABL* gene. Patients who met the inclusion criteria received a self-assessment questionnaire. They were fully informed about the study procedure and received an informational document. Patients who did not return the questionnaire and those whose data were lost received a phone call to gather information. Data collection was carried out by the IUCT-O, and data processing was performed by research unit UMR 1027 in Toulouse. After receipt of the self-assessment questionnaire at the time of diagnosis, new data were gathered at each medical consultation. These were scheduled as follows: every 3 months during the first year and every 6 months during the second year after diagnosis. During these consultations, data were gathered concerning treatments prescribed for CML; other treatments; Sokal risk score at diagnosis; evolution of hematologic/cytogenetic/molecular responses (the "optimal patient response to TKI" was defined according to these variables) [9]; and declared adverse drug reactions (ADR; patients were asked to report the existence or absence of ADRs in accordance with the Common Terminology Criteria for Adverse Events (CTCAE) version 5 classification, and their precise type) [10]. The study was approved by the "*Comité d'Ethique de la Recherche des Hôpitaux de Toulouse*" (Ethical Committee of Research, Toulouse University Hospital). Two populations of patients were defined: those who reported modifications in their professional activity during the study were assigned to the Acti-Pro+ group and those who did not report any modification were assigned to the Acti-Pro− group.

The primary endpoint was to determine the professional status of patients, represented by the rate of patients working versus patients on sick leave or receiving a disability pension (i) at time of diagnosis, (ii) after 1 year of therapy, and (iii) after 2 years of therapy. We also aimed to assess absenteeism and practical arrangements associated with the return to work. The self-assessment questionnaire was designed to collect the following patient data: marital status; socioeconomic category according to the *Institut National de la Statistique et des Etudes Economiques* or INSEE (French National Institute for Statistical and Economic Studies); profession; employment status (seeking a job, receiving disability pension, working); work organization and its modifications; and periods of sick leave. The self-administered questionnaire is provided in Online Resource 1.

All statistical analyses were performed using GraphPad Prism 6.0©. A descriptive analysis was performed, with the results expressed as mean ± SD for quantitative data. Quantitative data were assessed for normal distribution. Comparisons of quantitative data were made using Student's *t* test or Wilcoxon's rank sum test. Qualitative data were described as number of cases (%). Comparisons of percentages were undertaken by the chi-square test and Fisher's exact test, according to the expected number of cases. Associations were analyzed through univariate logistic regression. The limit of statistical significance was 0.05.

Results

A flow chart describing the study population is shown in additional data provided in Online Resource 2. In all, 115 patients met the inclusion criteria out of 150 patients identified with CML diagnosed between 01 January 2009 and 31 December 2014 at Toulouse University Hospital. Of these, 100 patients completed the self-assessment questionnaire and sent it back, with 66 reporting professional activity within

2 years after their diagnosis. Among these patients, 60 were working at the time of diagnosis, 2 were students, and 4 were seeking a job. Two years after the diagnosis, 43 patients had faced modifications in their professional activity due to CML or ADR to treatments (Acti-Pro+ group), and 23 patients did not report any impact of CML or its treatment on their occupational activity (Acti-Pro− group).

Table 1 shows the medical characteristics of the patients (Acti-Pro+ and Acti-Pro−). At the time of diagnosis, 86% ($n = 57$) of the patients reporting professional activity or seeking a job were in a chronic phase of CML, and imatinib was the first-line treatment for 55% of these patients ($n = 36$). We reported the existence of additional chromosomal aberrations (ACA). Three patients out of 66 were ACA Philadelphia-chromosome positive (ph+) (two in the Acti-Pro+ group and one in the Acti-Pro− group). The Sokal risk score was determined for 34 patients at diagnosis and averaged 1.56. Within 2 years after diagnosis, 65.2% (95% CI, 53.7–76.7) of patients had faced modifications in their professional activity ($n = 43$; Acti-Pro+ group); whereas, 34.8% (95% CI, 15.3–54.3) of patients did not report any impact on their occupational activity ($n = 23$; Acti-Pro− group). We compared patient characteristics from the Acti-Pro+ and Acti-Pro− groups. At the time of diagnosis, patients who reported modifications to work organization (Acti-Pro+ group) were more likely to have comorbidities than patients in the Acti-Pro− group (83.7% vs 47.8%,

Table 1 Medical characteristics of CML patients engaged in professional activity after diagnosis

	Patients with professional activity at the time of diagnosis	Acti-Pro+ group	Acti-Pro− group	*p*
Number of patients, *n* (%)	66 (100)	43 (65.2)	23 (34.8)	
Past medical history, *n* (%)	47 (71.0)	36 (83.7)	11 (47.8)	*0.0008***
Number of comorbidities, median (min-max)	1 (0–6)	2 (0–5)	0 (0–3)	*0.0006****
Charlson score, median (min-max)	0 (0–4)	0 (0–4)	0 (0–3)	0.1708
Circumstances of diagnosis of CML, *n* (%)				
Incidental	24 (36.0)	15 (34.9)	9 (39.1)	0.5189
Systematic medical checkup	19 (29.0)	14 (32.6)	5 (21.7)	0.1186
Symptoms	23 (35.0)	14 (32.6)	9 (39.1)	0.4117
Phase of the disease, *n* (%)				
Chronic	57 (86.0)	37 (86.0)	20 (87.0)	0.3719
Accelerated	5 (8.0)	4 (9.3)	1 (4.3)	0.8947
First-line treatment, *n* (%)				
Imatinib	36 (55.0)	22 (51.2)	14 (60.9)	0.8591
Dasatinib	13 (20.0)	9 (20.9)	4 (17.4)	0.9752
Nilotinib	17 (26.0)	12 (27.9)	5 (21.7)	0.8647
Inclusion in a clinical trial, *n* (%)	45 (68.0)	29 (67.4)	16 (69.6)	0.3407
One year after diagnosis				
Dosage modification, *n* (%)	14 (21.2)	10 (23.3)	4 (17.4)	0.8565
Initiation of at least one second-line treatment, *n* (%)	8 (12.1)	4 (9.3)	4 (17.4)	0.4278
Optimal patient response to TKI, *n* (%)	44 (66.7)	28 (65.1)	16 (69.6)	0.2286
Level of BCR-ABL (% IS), median (min-max)	0.04 (0.00–29.00)	0.05 (0.00–4.70)	0.04 (0.00–29.00)	0.7832
Patients with persistent ADR, *n* (%)	40 (60.6)	30 (69.8)	10 (43.5)	0.2465
Number of persistent ADR, median (min-max)	1 (0–4)	1 (0–4)	0 (0–2)	*0.0284**
Two years after diagnosis				
Dosage modification, *n* (%)	5 (7.6)	3 (6.9)	2 (8.7)	0.7177
Initiation of at least one second-line treatment, *n* (%)	13 (19.6)	8 (18.6)	5 (21.7)	0.8856
Optimal patient response to TKI, *n* (%)	58 (87.8)	40 (93.0)	18 (78.3)	0.0815
Level of BCR-ABL (% IS), median (min-max)	0.01 (0.00–11.00)	0.01 (0.00–11.00)	0.01 (0.00–11.00)	0.6902
Patients with persistent ADR, *n* (%)	40 (60.6)	29 (67.4)	11 (47.8)	0.0634
Number of persistent ADR, median (min-max)	1 (0–5)	1 (0–5)	0.5 (0–2)	*0.0101**

The statistical significance level was set at 0.05

CML, chronic myeloid leukemia; *BCR-ABL*, breakpoint cluster region-Abelson; *ADR*, adverse drug reaction

* Statistically significant result

respectively; $p = 0.0008$); each patient also reported a larger number of comorbidities (2 vs 0 per patient, respectively; $p = 0.0006$). No significant differences were observed between the two groups concerning circumstances of diagnosis, the *Charlson* score, Sokal risk score at diagnosis, first-line treatment (imatinib, dasatinib, or nilotinib), participation in a clinical trial or, more surprisingly, phases of the disease.

The proportion of patients with persistent ADR did not differ significantly between the two groups, either 1 year after diagnosis or 2 years after diagnosis (despite a trend, 67.4% vs 47.8%; $p = 0.0634$). However, at 1 and 2 years after diagnosis for patients who reported ADRs, those from the Acti-Pro+ group reported a higher number of persistent ADRs compared to the Acti-Pro− group (at 1 year, median 1 [0–4] vs 0 [0–2], respectively, $p < 0.03$; 2 years, median 1 [0–5] vs 0.5 [0–2], respectively, $p = 0.0101$). The ADR effects reported after 1 year differed from those reported after 2 years in our study, as did the proportion of each ADR in both groups. One year after diagnosis, asthenia ($n = 12$, 27.9%) and musculoskeletal disorders ($n = 12$, 27.9%) were the ADRs most represented in the Acti-Pro+ group, whereas the proportion of gastrointestinal ($n = 3$, 13%), dermatological ($n = 3$, 13%), and musculoskeletal disorders ($n = 3$, 13%) was higher in the Acti-Pro− group. This trend persisted 2 years after diagnosis: musculoskeletal disorders appeared to be more prevalent than asthenia (27.9% vs 20.9%) in the Acti-Pro+ group. There were no significant differences reported between patients from the Acti-Pro+ and Acti-Pro− groups concerning modifications of treatment, or cytogenetic or molecular responses.

The social and professional characteristics of patients engaged in a professional activity or seeking a job at the time of diagnosis (Acti-Pro+ and Acti-Pro− groups) are reported in Table 2. Our study population comprised 39% of women and the average age was 46 years. No significant differences were found between the Acti-Pro+ and Acti-Pro− groups in terms of age, marital status, family status, social and professional categories, work organization, or working hours at the time of diagnosis. Forty-three patients reported modifications to their work organization within 2 years after diagnosis. They represent the Acti-Pro+ group.

As shown in Table 3, 36 of these patients (83.7%) reported work modifications in the first year after diagnosis, and this proportion tended to decrease with time as only 30 patients (69.8%) reported an impact after 2 years. Employment status (seeking a job, receiving a disability pension, working) was not radically different between the first and second years after diagnosis, as 12 patients reported a work modification after 1 year (27.9%) versus 13 (30.2%) after 2 years. Not surprisingly, the proportion of patients receiving a disability pension was greater after 1 year than after 2 years (8 vs 1 patient). Twenty-two patients (51.2%) reported modifications in work organization after 1 year versus 18 patients (41.9%) after 2 years. The prevalence of sick leave was greater after 1 year than after 2 years ($n = 20$, 46.5% vs $n = 10$, 23.3%, respectively). Among modifications to work organization, change in the number of working hours was the most represented (41.9% after 1 year, 18.6% after 2 years). Other modifications comprised changes in status (7.0% vs 4.7%) and in work pace (34.9% vs 32.6%).

Table 4 describes modifications to work organization. Within 2 years after diagnosis, 14 patients reported a change in work organization (32.6%). Among these changes are the following: 12 patients were prescribed a reduction in working hours, 5 had medical restrictions in work tasks, 2 reported a change in profession in the same company, and 2 were dismissed for medical reasons.

We compared self-reported difficulties of patients concerning their job performance. Among the 66 patients who were engaged in professional activity at the time of diagnosis, 33 (50.0%) reported having difficulties performing their work within 2 years of diagnosis. Twenty-eight of these patients reported modifications in work organization (Acti-Pro+ group), whereas five patients had difficulties but did not report any modification at work (65.1% of patients vs 21.7%, respectively; $p < 0.0001$). Hence, for patients with CML, there was a significant correlation between having difficulties in performing a job and modifications in work organization. Conversely, 15 patients faced modifications in work organization without self-reporting any difficulty in performing their job. In the Acti-Pro+ group, 24 patients (55.8%) reported having difficulties performing their job in the first year after diagnosis and 23 patients (53.5%) in the second year. Asthenia was the main obstacle faced by patients (24 patients in the first year, 19 patients in the second year). Other challenges comprised interpersonal difficulties, anxiety, and depressive disorder. These were equally reported in the first and second years.

Discussion

Our study showed that 65.2% of patients treated for CML reported an impact of the disease and/or its treatment on their professional activity. Among the modifications, change in the number of working hours was the most represented (41.9% after 1 year, 18.6% after 2 years). Other modifications comprised changes in status (7.0% vs 4.7%) and work pace (34.9% vs 32.6%). Within 2 years of diagnosis, 14 patients reported a change in work organization (32.6%). Among these changes are the following: 12 patients were prescribed a reduction in working hours, 5 had medical restrictions on work tasks, 2 reported a change in profession in the same company, and 2 were dismissed for medical reasons. CML remains a rare and chronic disease. Its once severe course has been dramatically improved by TKI treatments. In the last few years, a paradigm shift in the management of patients has occurred as molecularly targeted therapies have emerged. These new

Table 2 Social and professional characteristics of CML patients engaged in professional activity

	Patients engaged in professional activity	Acti-Pro+	Acti-Pro−	*p*
Number of patients, *n* (%)	66 (100)	43 (65.2)	23 (34.8)	
Women, *n* (%)	26 (39.0)	19 (44.2)	7 (30.4)	0.4754
Age at the time of diagnosis (years), median (min-max)	46 (20–62)	47 (20–62)	42 (23–59)	0.0736
Marital status, *n* (%)				
Married	38 (58.0)	26 (60.5)	12 (52.2)	0.3239
Divorced	3 (5.0)	3 (7.0)	0 (0)	0.2449
Widowed	2 (3.0)	1 (2.3)	1 (4.3)	0.6075
Single	12 (18.0)	7 (16.3)	5 (21.7)	0.4682
Partnership	11 (17.0)	6 (14.0)	5 (21.7)	0.3329
Dependent children, *n* (%)	33 (50.0)	21 (48.8)	12 (52.2)	0.505
Last obtained diploma				
Anterior to bachelor degree	28 (42.0)	20 (46.5)	8 (34.8)	0.5983
Bachelor degree	13 (20.0)	8 (18.6)	5 (21.7)	0.5832
Posterior to bachelor degree	22 (33.0)	12 (27.9)	10 (43.5)	0.1237
Social and professional category, *n* (%)				
Farmers	2 (3.0)	1 (2.3)	1 (4.3)	0.5291
Artisans, traders, and company directors	9 (14.0)	7 (16.3)	2 (8.7)	0.658
Managers and higher intellectual professionals	11 (17.0)	6 (14.0)	5 (21.7)	0.2048
Intermediate professionals	3 (5.0)	1 (2.3)	2 (8.7)	0.1619
Lower supervisory and technical occupations	30 (45.0)	22 (51.2)	8 (34.8)	0.2066
Workers	4 (6.0)	4 (9.3)	0 (0)	0.2157
Job applicants	4 (6.0)	1 (2.3)	3 (13.0)	0.0715
Students	2 (3.0)	1 (2.3)	1 (4.3)	0.6075
Others	7 (11.0)	2 (4.7)	5 (21.7)	0.135
Form of employment, *n* (%)				
Full-time	53 (80.0)	37 (86.0)	16 (69.6)	0.4136
90–80%	3 (5.0)	3 (7.0)	0 (0)	0.2887
70–50%	2 (3.0)	1 (2.3)	1 (4.3)	0.5291
Number of working hours per week, *n* (%)				
< 35 h	8 (12.0)	6 (14.0)	2 (8.7)	0.8111
35 h	15 (23.0)	12 (27.9)	3 (13.0)	0.415
35–40 h	15 (23.0)	9 (20.9)	6 (26.1)	0.9834
40–50 h	13 (20.0)	9 (20.9)	4 (17.4)	0.8695
> 50 h	8 (12.0)	5 (11.6)	3 (13.0)	0.5858

CML, chronic myeloid leukemia

therapies have demonstrated unprecedented efficacy, improving survival times and highlighting new challenges for patients who are now able to return to their former lives. Few studies have addressed the issue of return to work after treatment of the disease [6–8]. However, the professional dimension remains a crucial determinant of a patient's quality of life for economic, social, physical, and psychological reasons. Return to work is a key determinant of quality of life for patients with CML. The literature reveals that the ability to work among patients with CML is associated with higher scores on two scales evaluating quality of life: the Functional Assessment of Cancer Therapy-General (FACT-G) ($p < 0.001$) and the Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu) ($p < 0.001$) [7]. Work participation in a society can define an individual's self-worth, identity, and societal role, besides contributing to financial security. Returning to work after cancer treatment seems crucial for cancer survivors in maintaining a sense of normalcy and improving quality of life and control, while failure to maintain employment could deprive an individual of social contact and well-being [11, 12]. The same paradigm should certainly apply to CML patients, who remain on treatment their whole lives and have to live with the disease and its treatment. Majority of patients are still working at the time of diagnosis;

Table 3 The professional consequences of CML after diagnosis

	Acti-Pro+ $n = 43$ (100%)	
	One year after diagnosis	Two years after diagnosis
Modifications to work organization after diagnosis, *n* (%)	36 (83.7)	30 (69.8)
Modification in employment status, *n* (%)	12 (27.9)	13 (30.2)
Job applicants, *n* (%)	1 (2.3)	2 (4.7)
Without professional status, *n* (%)	1 (2.3)	1 (2.3)
Disability pension, *n* (%)	8 (18.6)	1 (2.3)
Professional activity, *n* (%)	1 (2.3)	8 (18.6)
Modification in professional activity, *n* (%)	22 (51.2)	18 (41.9)
Short period sick leave, *n* (%)	20 (46.5)	10 (23.3)

therefore, they simultaneously face the complexity and fear associated with the diagnosis of CML, their symptoms, information given by healthcare practitioners about treatment options, and social, financial, and professional challenges. For patients who are studying at the time of diagnosis, the question of whether they should continue their course might arise. Patients who are still working at the time of diagnosis might be concerned about their future ability to perform their occupational tasks [8] in the short and long term, the need for modifications to work organization, and the financial consequences of sick leave, dismissal, or retirement. At the time of diagnosis, 86% ($n = 57$) of patients engaged in a professional activity or seeking a job were in the chronic phase of CML. Not surprisingly, patients within a chronic but stable condition were more likely to work than patients facing an accelerated phase, this being associated with more aggressive symptoms and treatments and the need for more medical care. Only three patients were ACA ph+ (4.5%); this finding is consistent with Fabarius et al. who reported that 6.9% of patients were ACA ph+ in a cohort of CML [13].

In our study, two groups were identified: Acti-Pro+ (modifications in professional activity) and Acti-Pro− (no modification). The majority of patients reported modifications due to CML in their professional activity (Acti-Pro+, $n = 43$ vs Acti-Pro−, $n = 23$) within 2 years after diagnosis. This finding suggests a professional impact of CML and most importantly its treatment, as the majority of patients reported changes in their usual professional organization associated with their disease. The difference reported between the two groups in terms of ADR suggests they were the major factor affecting the occurrence of work modifications associated with CML treatments. The determinants associated with a greater risk of facing modifications in work organization were identified through comparison of the Acti-Pro+ and Acti-Pro− groups. Medical history and comorbidities were more likely to be found in Acti-Pro+ individuals. Modifications in work organization were more likely to happen when a patient was facing a medical history and complications of other diseases, as their physical and psychological resistance was already altered [4, 14]. Surprisingly, the phases of the disease (chronic and accelerated) were not significantly different between the groups. There is a possibility of a bias that might have underestimated our findings (limited number of patients), as a difference is to be expected between modifications in work organization between patients in the chronic phase of the disease and patients in the accelerated phase. Moreover, our results highlight the impact of ADRs on changes in work organization. One and 2 years after diagnosis, a greater number of persistent ADRs were found in the Acti-Pro+ than in the Acti-Pro− group. These findings suggest a role of ADR persistence in the reduction of quality of life among patients after diagnosis and treatment. The issue of symptom burden and quality of life among patients with CML has been addressed [15–17]. A study revealed that even though quality of

Table 4 The professional consequences of CML in terms of work organization after diagnosis

	Acti-Pro+ $n = 43$ (100%)
Long period sick leave within 2 years after diagnosis, *n* (%)	20 (46.5)
Work adaptation within 2 years after diagnosis, *n* (%)	14 (32.6)
Prescribed reduction in working hours, *n* (%)	12 (27.9)
Reduction in work tasks for physical reasons, *n* (%)	4 (9.3)
Reduction in work tasks for psychological reasons, *n* (%)	1 (2.3)
Change in profession in the same company, *n* (%)	2 (4.7)
Dismissal for medical reasons, *n* (%)	2 (4.7)

life scores for patients treated with imatinib were high, they were negatively correlated with general symptoms ($r = -0.612$, $p < 0.001$), CML-specific symptoms ($r = -0.513$, $p < 0.001$), and interference of symptoms ($r = -0.596$, $p < 0.001$) [15]. ADRs have a marked impact on a patient's life and seem to influence the ability to return to work. The nature of ADRs differs 1 and 2 years after diagnosis and between patients facing modifications at work and those who do not. Asthenia and musculoskeletal disorders remain the main ADRs reported by patients who face modifications at work. Asthenia is a major and common symptom of cancer in general [18]. A previous study reported chronic fatigue as one of the most important factors limiting health-related quality of life among CML patients [19]. Musculoskeletal disorders become more prevalent in the second year after diagnosis, as asthenia tends to diminish. Interestingly, there was no difference between the two groups in terms of the TKI prescribed, although the ADRs differed between the three frontline TKIs.

Expectedly, changes in work organization seemed to appear within the first year after diagnosis and to decrease afterwards. At the time of diagnosis, symptoms might be strong as the disease has not stabilized and musculoskeletal ADRs might be intense, making patients more vulnerable and less able to face their work tasks. As they receive treatment and recover their strength, they are more likely to be able to complete their work. For similar reasons, the proportion of patients receiving a disability pension and the prevalence of sick leave were greater after 1 year than after 2 years. We attempted to describe the different changes in work organization that patients reported facing. Among these, a change in the number of working hours was the most commonly reported, as it constitutes probably the first, most practical, reversible, and flexible change in terms of management. Medical restrictions imply the involvement of an occupational practitioner, a physician specialized in the interaction between employees' health and their work. The role of such practitioners is to prevent an alteration in patients' health due to work, occupational disease, and accidents at work. An occupational practitioner is legally allowed to prescribe medical restrictions on precise work tasks if posing a danger to an employee's health. In some cases, medical restrictions might be sufficient to protect an employee's health and avoid dismissal for medical reasons, which might lead to impoverishment and social peril for disabled employees. Studies have addressed the need for professional assistance and support services to keep patients in their professional lives [20, 21].

Finally, we compared self-reported difficulties of patients concerning their job performance. For patients with CML, there was a significant correlation between having difficulties performing a job and modifications in work organization. Conversely, 15 patients faced modifications in work organization without reporting any difficulty performing their jobs. This result suggests the existence of other reasons leading to changes in work organization.

Our study has a number of strengths. Our topic focuses on the professional impact of CML, a disease for which prognosis has dramatically improved, but leading to new questions and unmet medical needs. The professional impact of cancer is a determinant of recovery of a patient's quality of life, a current topic of interest. After obtaining authorizations, we designed a prospective methodology and focused on factors rarely studied in CML patients. We gathered medical, social, and professional data to compare groups and thus broaden the scope of our understanding. To our knowledge, no previous study in CML has investigated factors associated with the modification of employment while on therapy. However, this study also presents a number of limitations. First, this study was conducted by a single investigator. Second, information was self-reported by the patients themselves, which may be associated with recall bias. However, the updating of data during 2 years after diagnosis was performed by caregivers during medical visits, which allowed correction of mistakes identified. Finally, the number of patients was limited, constraining the weight of our conclusions.

Future research should focus on preventive measures that could be proposed to reduce the professional impact of CML. Patients should be medically and socially supported to adapt their work organization to their new physical and psychological conditions. The interaction between general practitioners, hematologists, and occupational practitioners could be developed to give patients the best chance of properly returning to work or maintaining their professional situation. Patients at risk of professional changes can be identified using determinants associated with a greater risk of facing limitations at work. Patients with a risk profile (for example, developing musculoskeletal ADRs) could benefit from specialized and focused assistance.

Conclusions

CML patients face challenges such as their professional and social reintegration after diagnosis and initial phase of treatment. We found that during the 2 years after diagnosis, 65.2% of patients had faced modifications in their professional activity due to CML or the effects of ADRs to treatments (Acti-Pro+ group); whereas 34.8% of patients did not report any impact on their occupational activity (Acti-Pro− group). Among modifications to work organization, change in the number of working hours was the most common. Other modifications comprised changes in status and in work pace. To the best of our knowledge, this study was the first to assess the impact of CML and its treatments on the professional activity of patients. Our findings increase our understanding of the determinants of work limitations associated with CML and provide

insights into the professional consequences of this disease. Work participation, as a key determinant of health-related quality of life, should be assessed systematically, and physicians' attention should be focused on ADRs at risk of causing working issues.

Authors' contributions SDB, FV, FD, FHu, and FHe created the study concept and design. CP, MG, MS, and FD performed the acquisition of data. SDB, FV, FHu, FD, JMS, ED, GL, and FHe performed the analysis and interpretation of data. SDB, FV, FHu, and FHe wrote the draft of the manuscript. FD, ED, JMS, GL, and FHu undertook critical revision of the manuscript. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval and consent to participate All procedures performed in the study that involved human participants were in accordance with the ethical standards of the institutional committee, national research committee, and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

Availability of data and material The datasets generated and analyzed during the study are available from the corresponding author on reasonable request.

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