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Research Paper

The survival of patients enrolled in a global direct-to-patient cancer medicine donation program: The Glivec International Patient Assistance Program (GIPAP)

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ABSTRACT

Background: The Glivec International Patient Assistance Program (GIPAP) is a unique direct-to-patient program that provides imatinib (Glivec) at no cost to eligible patients in low- and middle-income countries (LMICs) with chronic myelogenous leukemia (CML) or gastrointestinal stromal tumor (GIST). This paper analyses the output, outcome and impact of the program between 2001 and 2014 using the data collected by the Max Foundation.

Method: We extracted data on GIPAP patients' country of residence, sex, diagnosis, date of enrollment in GIPAP, age at enrollment, case closure date, and reason for closure from The Max Foundation database covering the period 2001 to 2014. We used Kaplan-Meier method to assess the survival rate of patients in GIPAP and used the proportional hazard regression model to estimate the effect of different variables on patients' survival.

Findings: About 63,000 GIPAP patients in 93 countries received over 71 million defined daily doses (DDD) of imatinib between 2001 and 2014. Our analysis showed that GIPAP patients had a 5-year survival rate of 89% which compares favorably to survival in high income countries despite the challenges of delivering cancer care in LMICs. Age at enrollment into the program, sex, duration between diagnosis and enrollment into program, year of enrollment, and patients' diagnosis (CML vs non-CML) were factors that influenced survival.

Interpretation: The GIPAP program has improved the survival of CML and GIST patients in LMICs, most of whom would not have had access to imatinib in the absence of the donation and therapeutic support of the program.

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1. Introduction

Chronic myeloid leukemia (CML) is a rare hematologic malignancy that globally affects between one and two per 100,000 people annually [1,2]. CML had a poor prognosis and a median survival of less than 5 years before 2001, but is now considered a chronic disease since the advent of targeted therapies such as imatinib (Glivec®) [1,3–5]. With the introduction of imatinib, five-year cumulative relative survival ratios of CML in Swedish patients younger than 79 years increased from 0.54 between 1994 and 2000 to 0.80 between 2001 and 2008 [6]. Similarly, the five-year survival rate of CML increased from 63% with interferon therapy to 88% with the introduction of imatinib in a cancer treatment center in the United States [7]. Furthermore, imatinib has fewer side effects compared with alternative treatments [3,8].

Despite the improved outcomes for CML patients that have been treated with imatinib, the average monthly cost of $2500–$3500 USD in high income countries could limit its use in low- and middle-income countries (LMICs) [9]. This led Novartis in 2001 to establish the Glivec International Patient Assistance Program (GIPAP) to assist patients in LMICs not able to afford treatment [1,9].

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Research in Context

Evidence before this study

Glivec International Patient Assistance Program (GIPAP) has the largest database of chronic myeloid leukemia patients receiving imatinib in low- and middle-income countries (LMICs). Previous studies using the GIPAP data have examined institutional factors related to patient enrollment and outcomes, regional variations in age at diagnosis, and three-year survival rates of GIPAP patients. However, none of the studies has examined the medium- to long-term (five to seven years) survival of GIPAP patients nor estimated the number of lives saved through the program.

Added value of this study

This paper examines the medium- to long-term survival of GIPAP patients and estimates the number of lives saved through the program using routinely collected GIPAP program data.

Implications of all the available evidence

The short (one year) and medium- to long-term (five to seven years) impact of GIPAP program on survival of CML patients is excellent, and unadjusted for patients' prognosis at time of diagnosis, compares favorably to survival in high-income countries, despite the challenges of delivering cancer care in LMICs.

The Glivec International Patient Assistance Program (GIPAP) is a global program that was established by Novartis Pharma AG in 2001 and implemented in partnership with The Max Foundation and Axios International, to provide imatinib (Glivec) at no cost to eligible patients with CML or gastrointestinal stromal tumor (GIST) [1,10]. Eligible patients include Philadelphia chromosome-positive CML or c-kit (CD117) positive GIST patients who were not insured, not reimbursed, or could not pay for the treatment privately and were in countries that have minimal reimbursement capabilities and where regulatory approval or at least an import license for Glivec for CML/GIST had been obtained [11–13].

Using a direct-to-patient approach, GIPAP involves different levels of partners – patients, patients' physicians, implementing partners, and Novartis. Each of the partners plays specific roles that ensure the success of the program. Novartis identified the countries where the programs would be implemented and collaborated with The Max Foundation to select qualified institutions and physicians in these countries. It also supplied the requested amount of imatinib to the cancer treating institutions and contracted with Axios International to deal with supply logistics in countries where the company lacked the necessary logistics in-country to support drug importation [1].

The Max Foundation conducted socioeconomic evaluation and verified the eligibility of patients, in addition to requesting product donation delivery from Novartis at three-month intervals based on individual patient's physician prescription. The Max Foundation also supported patients' adherence to medications by providing peer-to-peer support and supported by Novartis and others, also engaged in CML educational initiatives and awareness campaigns [1,2]. Additionally, The Max Foundation and Axios International maintained databases of data from different patients and institutions involved in the program [9]. Axios International apart from managing the drug import process in some countries, supported interaction with GIPAP physicians and institutions in countries where Novartis did not have a presence to ensure that they followed correct procedures [13,14].

The physicians in GIPAP institutions diagnosed the patients and made a request to The Max Foundation for the patients to be enrolled in the program. There were no limits to the number of patients eligible for GIPAP in any participating institution or country. Participation of physicians was voluntary, but they played an important role in the success of the program [1,2]. The patients' physicians worked with the implementing partners to ensure that the patients received the appropriate doses they needed at the appropriate time. The physicians were also responsible for managing and reviewing enrolled patients quarterly. If a patient did not come for the quarterly review and attempts by The Max Foundation to locate the patient failed, such a case was considered as "closed" or non-active, and could be re-instated into the program if contact was re-established [2]. In addition, the physicians and nurses had to comply with the demanding data entry needs of the program by filling out reports for each patient quarterly that were collected and validated by The Max Foundation [1,2]. To ensure adherence to the medication, which has been shown to correlate with improved survival, the physicians also contacted patients with appointment reminders and other necessary information [1].

Previous studies using the GIPAP data have examined institutional factors related to patient enrollment and outcomes [9], regional variations in age at diagnosis and survival of GIPAP patients [15], and three-year survival rates of GIPAP patients [2,15]. However, none of the studies has examined the medium- to long-term survival of GIPAP patients nor estimated the number of lives saved through the program.

This paper examines the medium- to long-term survival of GIPAP patients and estimates the number of lives saved through the program using routinely collected GIPAP program data. This paper also reports the outputs and outcomes of the GIPAP program using the Boston University Access to Medicines Metrics Framework developed as part of the Access Accelerated initiative [16,17]. The Boston University Access to Medicines Metrics Framework consists of a taxonomy of 11 global health program strategies such as medicine donation and price schemes, with the corresponding logic models designed to report inputs, activities, outputs, outcomes, and impacts of pharmaceutical industry led global health programs [16].

2. Methods

2.1. Data sources

We extracted data on patients' country of residence, sex, diagnosis, date of enrollment in GIPAP, age at enrollment, case closure date, and reason for closure from The Max Foundation database covering the period 2001 to the end of 2014. The analysis included data from 93 countries that were involved in GIPAP between 2001 and 2014. This also includes patients enrolled in the Novartis Oncology Access (NOA) program in India who were receiving free imatinib, referred to as NOA-GIPAP patients. However, for the purposes of this paper, we will collectively refer to both the GIPAP and NOA-GIPAP patients as GIPAP patients.

2.2. Variables

We calculated the total daily doses of imatinib donated to GIPAP patients by Novartis by dividing the total volume of medicine donated in milligrams by the defined daily dose (DDD) of imatinib. Since no DDD for imatinib has been established by the World Health Organization [18], we used a DDD of 400 mg which is the modal daily dose of imatinib taken by GIPAP patients.

$$\textit{Total daily doses of imatinib donated} = \textit{Volume of imatinib donated in milligrams} / \textit{defined daily dose of imatinib}$$

The potential number of CML patients saved by GIPAP in five years was calculated by subtracting the estimated number that survived

after 5 years from the number expected to survive after 5 years in the absence of imatinib [7].

Potential number of CML patients saved by GIPAP in 5 years = Estimated number that survived after 5 years − Number expected to survive after 5 years in the absence of imatinib.

2.3. Statistical analysis

We did descriptive statistics using sums, means and standard deviations for continuous variables and percentages for categorical variables. We used Kaplan-Meier method to assess the survival rate of patients in GIPAP. Our event of interest was death of patient, while closure due to other reasons such as loss to follow-up, and patients that were still alive at the end of 2014, were analyzed as censored data. Additionally, we conducted a sensitivity analysis with the assumption that patients that were lost to follow-up had all died at the point they were lost to follow-up. We also systematically conducted sensitivity analyses without data from India and China (both countries contributed about 50% of GIPAP patients), to see if different results would be obtained. We used Wilcoxon and Log-Rank tests to assess whether short- (one year) or long-term differences (five to seven years) exist in survival between patients with CML diagnosis and those with non-CML (mostly gastrointestinal stromal tumor) diagnosis, and between males and females. Furthermore, we used a proportional hazard regression model to estimate the effect of sex, diagnosis (CML vs non-CML), age at enrollment in GIPAP, time in months from diagnosis to enrollment in GIPAP, and year of enrollment, on patients' survival.

The estimated number of GIPAP CML patients that survived after five years was calculated by multiplying the five-year survival rate in GIPAP CML patients by the number of patients enrolled in the program. The number expected to survive after five years in the absence of imatinib was calculated by multiplying the 1982–1997 five-year survival rate of 650 CML patients receiving treatment in a cancer treatment center in the United States (63%) by the number of people enrolled in the program [7]. The 1982–1997 five-year survival rate was used to calculate the expected number of patients that would have survived in the absence of imatinb because it was one of the most recent published five-year survival rate of CML prior to the approval of imatinib in 2001 [7]. The graph of patients enrolled in GIPAP was performed using Microsoft Excel and SAS 9.4 software package (SAS Institute Inc., Cary, NC, USA) was used for all other statistical analysis.

2.4. Role of the funding source

The study sponsor had no role in the study design; collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the paper for publication. The authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

2.5. Data statement

The dataset analyzed for this publication is available on request.

3. Results

3.1. Descriptive analysis

The characteristics of the patient population is shown in Table 1. The majority of GIPAP patients were males (61%). About 85% of the patients were treated for CML, 14% for GIST and 1% for other indications such as Philadelphia chromosome-positive acute lymphocytic leukemia (Ph+ ALL) and systemic mastocytosis. For the CML patients, 87% were in the chronic stage of the disease at diagnosis, 8% in the accelerated stage and 5% in the blast stage. The mean and median age of patients at enrollment into GIPAP were both 41 years, with a median interquartile range of 22 years, and the mean duration from disease diagnosis to enrollment in GIPAP was 10 months. The mean and median duration of patient follow-up was 41 and 30 months respectively with a median interquartile range of 51 months.

Table 1
Descriptive analysis of patients enrolled in GIPAP 2001–2014.

Variable	Frequency	Percentage
Sex		
Male	38,432	60.64%
Female	24,948	39.36%
Diagnosis		
CML	53,878	85.01%
GIST	8986	14.18%
Others (e.g. Ph positive ALL; systemic mastocytosis)	517	0.81%
Stage of CML disease		
Chronic	46,752	86.78%
Accelerated	4522	8.39%
Blast Crisis	2601	4.83%
	Mean	**Standard deviation**
Age at diagnosis (years)	40.57	15.39
Age at enrollment into GIPAP (years)	41.47	15.40
Time between diagnosis and enrollment in GIPAP (months)	10.33	23.83
Duration of patient follow up (months)	40.74	34.70

Our trend analysis of new patients ever enrolled in GIPAP in 93 countries showed a progressive increase in the number of new patients enrolled in GIPAP from 2001 to 2007, a decline in 2008 and a fairly constant number from 2009 to 2014 (Fig. 1). The total enrolled patients increased from 12 in 2001 to 63,381 in 2014.

3.1.1. Program outputs

GIPAP provided imatinib to more than 63,000 patients in 93 LMICs between 2001 and 2014. Novartis donated about 72 million DDD and 66 million treatment days of imatinib to patients enrolled in GIPAP during that time.

3.1.2. Survival rates

Our survival analysis of all GIPAP patients enrolled from 2001 to 2014 shows a one-, three, five- and seven-year survival rate of 95%, 92%, 89% and 87%, respectively (Table 2).

Our disaggregated analysis showed that the short- ($p < 0.0001$) and long-term ($p < 0.0001$) survival rates of CML patients were significantly higher than those of non-CML patients. The one-, three-, five- and seven-year survival rates for CML patients were 96%, 92%, 90% and 88% respectively compared to 95%, 90%, 86%, and 79% for GIST patients (Table 2) (Fig. 2).

The disaggregated survival analysis of CML patients in different phases of disease at diagnosis showed that those diagnosed in the chronic phase had the best survival while those diagnosed in the blast phase had the worst survival. The one-, three-, five- and seven-year survival rates for chronic phase CML patients were 97%, 95%, 92% and 90% respectively compared to 89%, 83%, 80%, and 78% for accelerated phase and 69%, 59%, 56% and 53% for blast phase (Table 3) (Fig. 3).

The proportional hazard regression showed that the risk of death in non-CML patients was 24.6% higher than in CML patients ($p < 0.0001$), after adjusting for sex, age at enrollment into GIPAP, time between diagnosis and enrollment into GIPAP and year of enrollment.

Similarly, the result of the proportional hazard regression of GIPAP CML patients showed that the risk of death in male patients was seven percent higher than those of female patients ($p = 0.0308$), after adjusting for CML phase at diagnosis, age at enrollment into

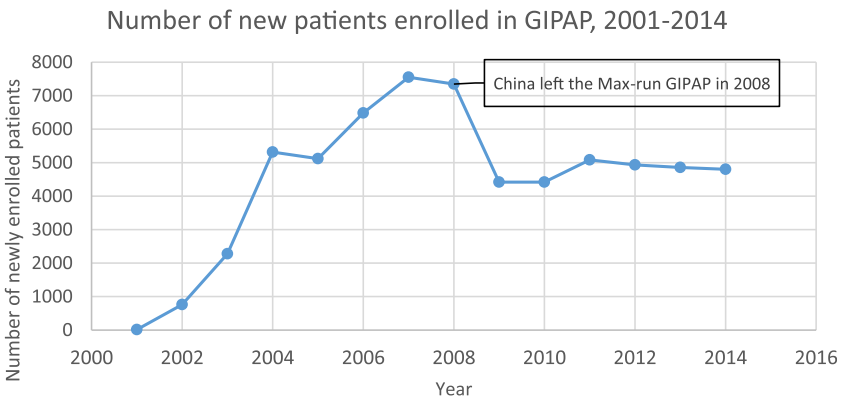

Fig. 1. Number of new patients enrolled in GIPAP 2001–2014.

GIPAP, time between diagnosis and enrollment into GIPAP and year of enrollment (Table 4).

With each year increase in age at enrollment into GIPAP, the risk of death in CML patients increases by 1.7%, holding other variables constant ($p < 0.0001$). In addition, with each month increase in the time between diagnosis and enrollment into GIPAP, the risk of death in CML patients increases by 0.4%, holding other variables constant ($p < 0.0001$). For each year increase in the year of enrollment, the risk of death decreased by 3.5%, which means that those enrolled in the later years of the program had a better survival rate. The risk of death was 163% and 744% more likely in CML patients diagnosed at the accelerated or blast phase, respectively, compared to those diagnosed at the chronic phase.

The estimated five-year potential number of CML patients saved by GIPAP (see formula for calculation in the methods section) is 17,107.

3.1.3. *Sensitivity analysis*

Our sensitivity analysis based on the assumption that all the cases lost to follow-up (12,679 patients) died at the time they were lost to follow-up shows a one-, three-, five- and seven-year survival rate of 90%, 77%, 67%, and 57%, respectively (Table 5). The five-year potential number of CML patients saved by GIPAP based on this assumption will be 2757.

We also conducted sensitivity analyses without data from India and China (both countries contributed about 50% of GIPAP patients), to see if different results would be obtained. The analysis showed a one-, three-,

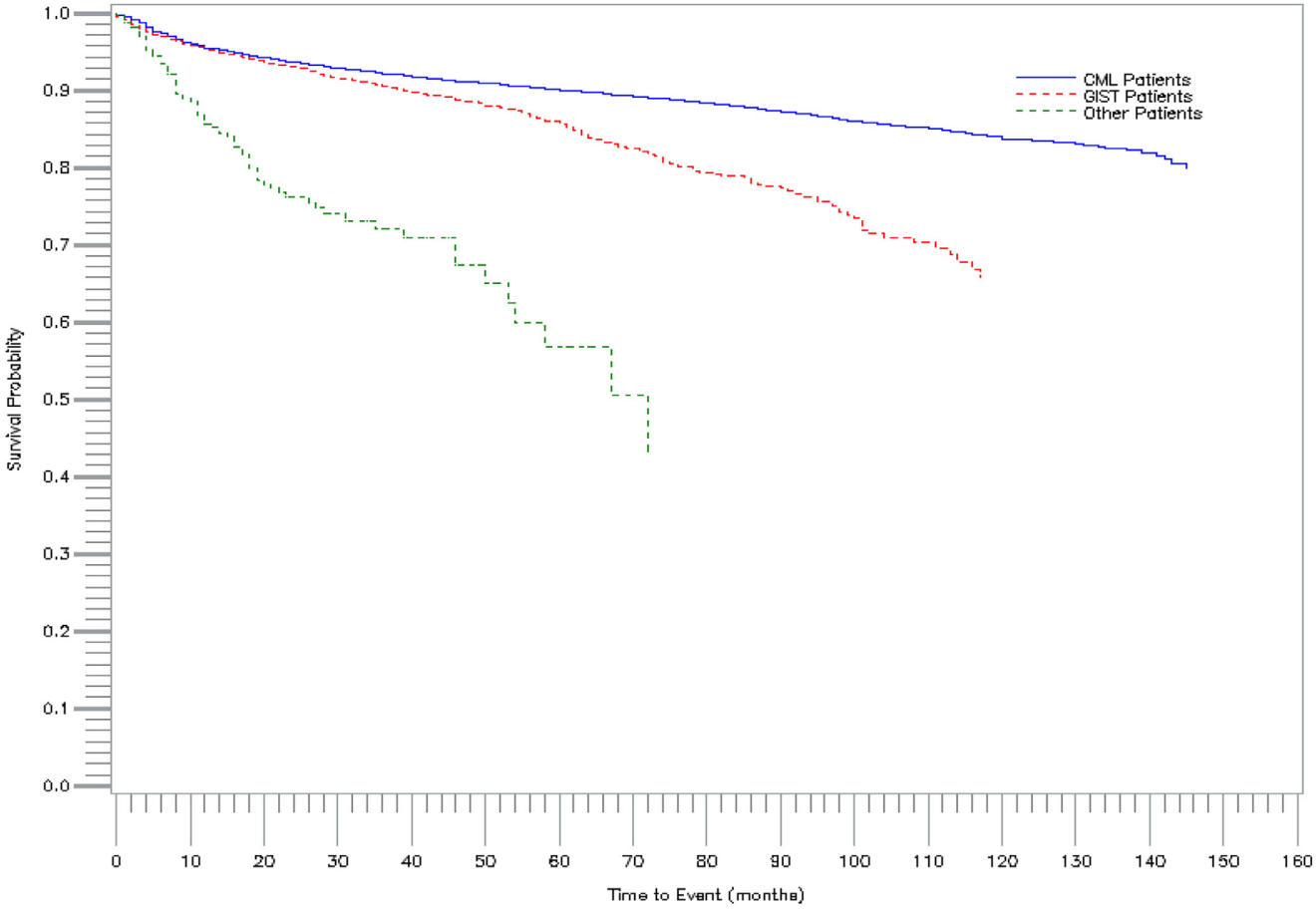

Fig. 2. Disaggregated Kaplan–Meier Survival analysis of GIPAP patients, showing survival rate of CML, GIST and other non-CML patients 2001–2014.

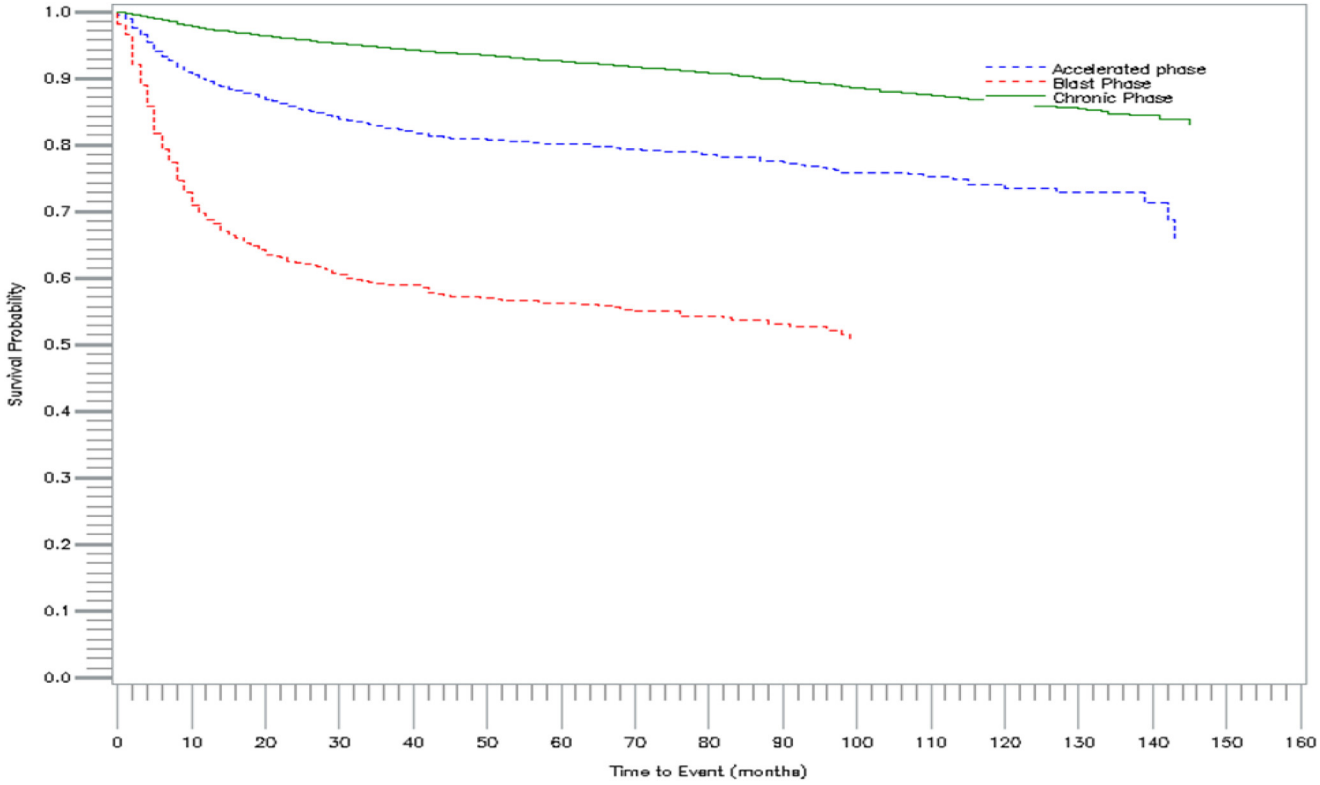

Fig. 3. Disaggregated Kaplan–Meier survival analysis of GIPAP CML patients, showing survival rate of CML patients in the chronic, accelerated and blast phases at diagnosis, 2001–2014.

Table 2
Kaplan–Meier survival analysis of GIPAP patients 2001–2014.

	Number at risk: all patients	Survival rate: all patients (95% CI)	Number at risk: CML Patients	Survival rate: CML patients (95% CI)	Number at risk: GIST patients	Survival rate: GIST patients (95% CI)	Number at risk: other[a] patients	Survival rate: other[a] patients (95% CI)
One year	47,887	95.40% (95.23–95.57)	41,853	95.50% (95.32–95.68)	5808	95.25% (95.73–94.77)	226	85.69% (89.36–82.02)
Three year	28,270	91.88% (91.63–92.13)	25,915	92.16% (91.90–92.42)	2288	90.48% (91.30–89.66)	70	72.09% (78.09–66.09)
Five year	17,025	89.49% (89.18–89.80)	15,988	89.99% (89.67–90.31)	1021	85.59% (86.90–84.28)	18	56.78% (68.40–45.16)
Seven year	9068	87.13% (86.74–87.52)	8667	87.79% (87.39–88.19)	374	78.66% (80.80–76.52)		

[a] Other patients include: hypereosinophilic syndrome/chronic eosinophilic leukemia, dermatofibrosarcoma protuberans, myelodysplastic syndromes/myeloproliferative disorder, systemic mastocytosis, and Ph positive ALL patients.

Table 3
Disaggregated Kaplan–Meier survival analysis of GIPAP CML patients, showing survival rate of CML patients in the blast, accelerated and chronic phase at diagnosis, 2001 – 2014.

	Number at risk: BP patients	Survival rate: BP patients (95% CI)	Number at risk: AP patients	Survival rate: AP patients (95% CI)	Number at risk: CP patients	Survival rate: CP patients (95% CI)
One year	1038	68.81% (70.81–66.81)	3142	89.46% (90.40–88.51)	37,671	97.40% (97.55–97.25)
Three year	455	58.99% (61.42–56.56)	1713	82.53% (83.82–81.24)	23,747	94.59% (94.83–94.35)
Five year	235	56.05% (58.74–53.37)	948	80.03% (81.49–78.57)	14,797	92.44% (92.75–92.13)
Seven year	123	53.14% (56.30–49.98)	471	77.52% (79.32–75.72)	8013	90.33% (90.73–89.93)

AP: accelerated phase CML, BP: blast phase CML, chronic phase CML.

Table 4
Result of the proportional hazard regression of GIPAP CML patients 2001–2014.

Parameter	Parameter estimate	Standard error	Hazard ratio (95% CI)	*p*-value
Age at enrollment into program	0.01689	0.00104	1.017 (1.019–1.015)	<0.0001
Duration between diagnosis and enrollment into program (months)	0.00434	0.00040	1.004 (1.005–1.004)	<0.0001
Enrollment year	−0.03529	0.00562	0.965 (0.976–0.955)	<0.0001
Sex (males vs females)	0.06732	0.03117	1.070 (1.137–1.006)	0.0308
Disease phase at diagnosis (accelerated vs chronic)	0.96526	0.04329	2.625 (2.958–2.412)	<0.0001
Disease phase at diagnosis (blast vs chronic)	2.13341	0.04128	8.444 (9.155–7.787)	<0.0001

Table 5
Sensitivity analysis based on assumption that all the cases lost to follow-up died at the time they were lost to follow-up.

	Number at risk: all patients	Survival rate: all patients (95% CI)	Number at risk: CML patients	Survival rate: CML patients (95% CI)	Number at risk: non-CML patients	Survival rate: non-CML patients (95% CI)
One year (12 months)	47,695	90.05% (89.80–90.30)	41,682	90.15% (89.89–90.41)	6013	89.52% (88.85–90.19)
Three year (36 months)	28,168	76.90% (76.52–77.28)	25,825	77.33% (76.93–77.73)	2343	73.29% (72.08–74.50)
Five year (60 months)	16,940	66.55% (66.08–67.02)	15,910	67.35% (66.86–67.84)	1030	58.21% (56.48–59.94)
Seven year (84 months)	9025	57.44% (56.88–58.00)	8626	58.48% (57.89–59.07)	399	45.21% (43.01–47.41)

five-, and seven-year survival rates of 95%, 91%, 89%, and 87% respectively which are similar to the survival rates in the main analysis.

4. Discussion

Our analysis showed a progressive linear increase in the number of new patients enrolled in GIPAP from 2001 to 2007 with a dip in 2008 (Fig. 1). This dip in the linear trend of number of new enrollees in 2008 was because Chinese GIPAP patients left GIPAP program in 2008 to join the China patient assistance program.

Our study also found that the three and five-year survival of CML patients in GIPAP (92% and 90% respectively), unadjusted to patients' prognosis at diagnosis, were similar to survival rates of CML patients on imatinib in other settings [19,20]. This shows that despite the limitations in providing cancer care in resource constrained settings in LMICs, GIPAP patients do as well as patients in high income countries. A 2005–2007 analysis of 13,568 GIPAP CML patients across 15 countries by Kanavos et al. [2] showed a minimum three years survival of 67% which is consistent with the survival rate in our sensitivity analysis [2]. While we calculated the "survival rate" in our main analysis, Kanavos et al. calculated the "minimum survival rate", defined as the proportion of patients who were still active in GIPAP after three years. So patients who were lost to follow up, those who left GIPAP and were receiving imatinib through other sources or those who switched to other treatments options were regarded as "dead" for the purposes of calculating the minimum survival rate. Conversely, to calculate the survival rate, our event of interest was patients who were confirmed as dead and we made adjustments in the Kaplan-Meier survival analysis for those patients who had not died by the time they left GIPAP for any reason.

The survival of GIST patients in our study, though less than that of CML patients, was similar to the survival of patients with operable GIST who received imatinib post-surgery [21]. However, the survival was higher than the five year survival rate of 55% seen in patients diagnosed with advanced GIST (who are more similar to GIST patients in GIPAP) in a previous study [22]. One reason for this disparity might be due to the small sample size (147 patients) in the earlier study.

Furthermore, we observed that for each year increase in the year of enrollment, the risk of death in CML patients decreased by 3.5% after adjusting for CML phase at diagnosis, age at enrollment into GIPAP, and time between diagnosis and enrollment into GIPAP, meaning that those enrolled in the later years of the program had a better survival rate. This improvement in survival might be due to physicians improved experience with the use of imatinib and better monitoring and supportive care of GIPAP patients. The roll out of GIPAP was observed to have catalyzed the improvement of health care infrastructure and local resources needed to diagnose, monitor, and support patients in the countries where GIPAP operated [1]. The important role of The Max Foundation in monitoring and providing support to patients, caregivers and physicians cannot be underestimated.

We found that the risk of death from CML was slightly higher in males than females. This is consistent with other studies that have identified the female gender as a favorable prognostic factor in CML survival [23–25]. The reason for the improved CML survival in women is uncertain [26]. In our study, age at diagnosis, which could affect survival, were similar for males (40 years) and females (41.5 years). We do not have data on patient's medication compliance and whether it was different for males and females which if different might explain the difference in survival. However, improved female gender survival has also been reported for some other hematological cancers such as acute myeloid leukemia [27] and acute lymphoblastic leukemia [28,29].

Additionally, our study showed that younger patients survived better than older ones. This is consistent with other studies that have shown that younger CML patients have better prognosis than older ones [30]. Old age was a major prognostic factor for CML survival prior to the introduction of imatinib but now, age only has marginal significance on survival and mainly with very old patients [31].

We estimated that the five-year potential number of CML patients saved by GIPAP is 17,107. We believe the estimated number of patients saved is a conservative estimate of the potential number of lives saved by the GIPAP program for two reasons. First, the baseline data of CML survival rate prior to the introduction of imatinib used in our calculation was from a high-income country. We expect that the baseline survival in the LMICs where GIPAP operates would be lower than what we used in our calculation. Second, the patients in GIPAP are poor patients who cannot pay for treatment privately and who do not benefit from any reimbursement or insurance scheme [12]. These are patients who without GIPAP might not be able to afford alternative cancer medications and so might have a far lower survival rate without GIPAP.

Our sensitivity analyses without data from India and China (both countries contributed about 50% of GIPAP patients), showed similar survival rates to the main analyses. This means that the survival of GIPAP patients in China and India were similar to those in the other 91 countries. This makes us to believe that the survival rate of GIPAP patients in this study can be generalized to other LMICs not included in the 93 countries if the programs are implemented in a similar fashion.

Although GIPAP has saved lives, one challenge of donation programs like GIPAP is program sustainability. Currently, it is recommended that patients on imatinib should continue indefinitely and this causes sustainability challenges [19]. To maintain sustainability, Novartis in 2009 started the NOA in countries with a growing middle class to provide imatinib at reduced prices to patients [1]. Under NOA, Novartis shares the cost of imatinib with the government (as in China), other payers, or individual patients (as in India and Philippines). In 2017, Novartis and The Max Foundation initiated the transition of the GIPAP program to CMLPath to Care™ a model where Novartis supports The Max Foundation with product donations and funding, and The Max Foundation independently distributes donations to qualified institutions for approved patients under the umbrella of its Max Access Solutions. CMLPath to Care continues to provide access to imatinib to qualified patients in 65 countries and additionally provides donations of nilotinib to qualifying patients in 39 countries as of December 2018. This new collaboration model has allowed The Max Foundation to open the partnership to other manufacturers, makers of tyrosine kinase inhibitors (TKIs) and other oral cancer medications. In 2017 Pfizer, Bristol-Myers Squibb, Takeda and Incyte had established similar collaborations with The Max Foundation under the umbrella of Max Access Solutions making available eight compounds, three of which provide second and third line treatments for CML, two provide first and second line for GIST, and others

support patients with renal cell carcinoma, and AKL positive lung cancer. As one of the benefits of the new model, at the end of 2017, partner clinicians in 25 countries were able to prescribe and have access to all TKIs approved elsewhere for the treatment of CML.

It is important to note that there are limitations in this study. First, the data used for this analysis were routine program data that was not collected for the purposes of program evaluation and so there are gaps in the data such as absence of certain clinical and socio-demographic data of patients which limited the extent of the analysis. Secondly, there was no follow-up survival data for patients who left GIPAP for any reason such as those who transferred to other patient assistance programs. However, we dealt with this limitation by modeling time contributed by patients that were lost to follow up as censored data in the Kaplan−Meier model. Thirdly, in calculating the number of lives saved through GIPAP we assumed that all the patients receiving care through GIPAP would not have had access to imatinib in the absence of the program. Although this assumption might not be true for every single patient, we believe that for almost all patients this assumption is true because patients were enrolled into GIPAP only if they were not insured, not reimbursed, or could not pay for the treatment privately and were in countries that have minimal reimbursement capabilities.

Finally, we do not have information about the prognostic scores of GIPAP patients, such as Sokal risk score, at diagnosis [32,33]. Without adjusting for the prognosis of the patients at diagnosis, comparing the survival of GIPAP patients with survival of patients from high income countries becomes challenging. Considering that the median age of GIPAP patients at initiation of treatment (41 years) was lower than those seen in high income countries would place GIPAP patients at a lower risk score with better prognosis. In the absence of a prognostic score at diagnosis, the best conclusion we can make from our study is that the survival of GIPAP patients is excellent, and unadjusted for patients' prognosis at time of diagnosis, compares favorably to survival in high income countries.

5. Conclusions

Glivec International Patient Assistance Program (GIPAP) has implemented a direct-to-patient drug donation model overseen by patients' oncologists. The program outputs are about 63,000 patients in 93 countries who received over 71 million defined daily doses of imatinib between 2001 and 2014. The impact of the program on survival showed a 5-year survival rate of 89 percent which is excellent, and unadjusted for patients' prognosis at time of diagnosis, compares favorably to survival in high income countries despite the challenges of delivering cancer care in LMICs.

Declaration of Competing Interest

David Tremblay works for Novartis Pharma AG and Pat Garcia-Gonzalez works for The Max Foundation. The Glivec International Patient Assistance Program (GIPAP) was established by Novartis Pharma AG and implemented in partnership with The Max Foundation.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2020.100257.

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