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The Economic Impact of Third Line Chronic Phase Chronic Myeloid Leukemia Treatment in Greece from a National Payer Perspective

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CONCLUSIONS

- The present analysis showed that ≥3L CML-CP can be expensive and still leads to complications, highlighting the need for an effective, tolerable, and cost-effective therapy for patients with resistance and/or intolerance to previous therapies.
- This was the first comprehensive COI analysis of ≥3L CML-CP in Greece, providing insights into the 3rd and later lines of treatment for patients with CML-CP, in the Greek setting.

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INTRODUCTION

- Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm with an incidence of 1-2 cases per 100,000 adults.[1,2]
- The introduction of tyrosine kinase inhibitors (TKIs) has transformed CML from a life-threatening blood cancer to a treatable disease.[2,3,4] However, TKI therapy in ≥3rd line (≥3L) treatment following prior resistance and/or intolerance is associated with increasing failure rates, progression risk and substantial economic burden.[2,5,6,7]
- In Greece, as per the 2018 national diagnostic and therapeutic protocol for CML, TKIs remain the preferred treatment across different lines of therapy, along with consideration of an allogeneic stem cell transplant based on patient profile. However, no specific TKI is recommended over the other for chronic phase CML (CML-CP) patients.[8] Hence, TKI cycling is often observed.[2,9,10,11]
- With limited published data on cost of CML in Greece, there is a lack of comprehensive understanding of cost-of-illness (COI) in patients with CML-CP undergoing ≥3L treatment.
- The aim of the study was to map the treatment patterns of CML-CP in patients who have received >2 TKIs, to investigate the disease related resource use, and to estimate the economic impact of CML-CP in Greece from the perspective of the national payer (National Organization for The Provision of Health Services, EOPYY).

METHODS

- A COI model was developed utilizing a prevalence-based approach for estimating the annual cost of ≥3L CML-CP over a 1-year time horizon in a real-world setting.
- Data for the prevalence of CML-CP in Greece were derived from the international publications and validated by Greece key opinion leaders (KOLs) due to the absence of published national epidemiological data.
- Using a semi-structured questionnaire, inputs on local treatment patterns and the resource used for the ≥3L treatment of CML-CP were gathered from three haematologists/ KOLs in the field of CML management **(Table 1)**.
- The estimated direct cost of the disease was calculated using a bottom-up approach i.e. by multiplying the total amount of each medical resource by its unit cost, and the total prevalent population.

METHODS (Continued)

- Only direct medical costs, reimbursed by EOPYY, were included in this analysis. The direct medical costs included in this COI model were categorized as follows:
  - Drug acquisition costs: Disease-specific treatment (TKIs), adverse events (AEs) treatment
  - Monitoring costs: Laboratory and imaging tests, physician visit (both for disease specific and AEs)
  - Hospitalization costs: Due to management of disease and AEs
- The unit costs per resource, such as hospital drug costs, official drug prices, hospitalization costs, physician visit costs and costs of laboratory and imaging tests, were collected from publicly available sources.
- All costs were calculated in Euros keeping the reference year as 2022.
- The acquisition cost for each drug regimen over a duration of 52 weeks (1-year) was determined by multiplying the proportion of patients receiving each treatment by the prevalent population, and its annual cost. Total monitoring costs were estimated by multiplying number of patients, annual test frequency, and their costs. Hospitalization costs for AEs were calculated by multiplying event rates and their management costs.

Table 1: Cost-of-illness model inputs

Epidemiology	Proportion of patients	Source
Greek Population	N=10,632,039	Eurostat Statistics[12]
Prevalence of CML patients	0.017%	Estimated from published literature[13,14,15] & KOLs' input
CML-Ph+ patients, %	95%	Canadian Cancer Society[15]
CML-CP Ph+ patients, %	95%	ESMO Clinical Practice Guidelines for CML, 2017[10]
CML treated patients in CP, %	95%	Novartis Market Research survey conducted in 2021 & KOLs' input
Prevalent patients with Ph+ in 1L treatment, %	66%	
Prevalent patients with Ph+ in 2L treatment, %	26%	
Prevalent patients with Ph+ in 3L+ treatment, %	8%	
Proportion of ≥3L CML-CP patients on different treatment regimens		
Treatment	**Proportion of patients**	**Source**
Nilotinib	25.0%	Weighted average usage based on Novartis Market Research and KOLs' input
Dasatinib	16.0%	
Bosutinib	16.0%	
Ponatinib	44.0%	
Annual frequency of monitoring tests in all ≥3L CML-CP patients*		
Monitoring tests	**Proportion of patients**	**Annual frequency**
Laboratory tests		
Blood count & Blood film exam	100%	Q2M
Blood chemistry test	100%	Q2M
Cytogenetic test		
Bone marrow aspiration	100%	One-off
Cytogenetic analysis (Karyotype)	100%	One-off
FISH	10%	One-off
RT-qPCR	100%	5 times per year
Mutational Analysis (NGS/Sanger)	30%	One-off
Imaging tests		
X-rays/Radiography	100%	Q12M, for Dasatinib Q4M
CT scan thorax	50%	Q12M
CT scan upper abdomen	50%	Q12M
CT scan lower abdomen	50%	Q12M
Electrocardiogram	100%	x3 per year, for Nilotinib & Ponatinib x7 per year
Annual frequency of physician visits**		
Type of visit	**Proportion of patients**	**Annual frequency**
Haematologist	100%	Every 3 months
Other physicians	70%	Twice a year (for Nilotinib & Ponatinib)

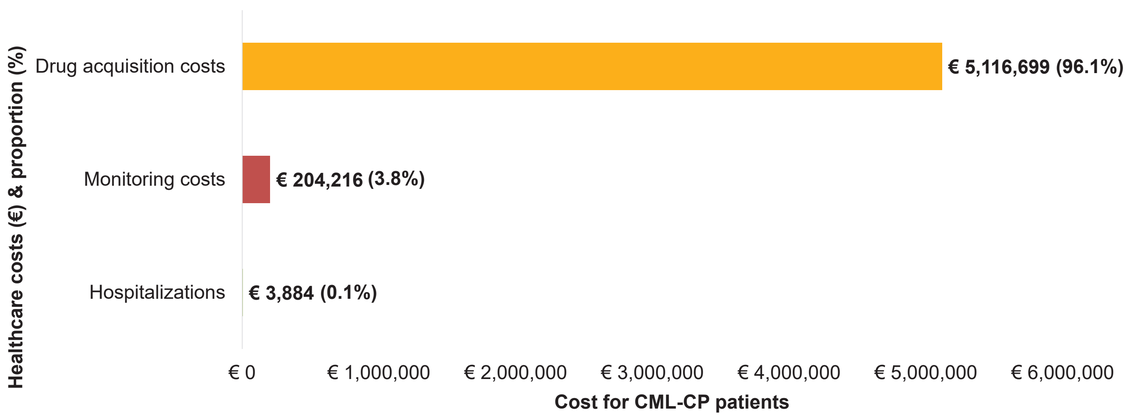
Abbreviations: CML: Chronic Myeloid Leukemia; CP: Chronic Phase; CT: Computerized Tomography; ESMO: European Society of Medical Oncology; FISH: Fluorescent in Situ Hybridization; KOLs: Key Opinion Leaders; Q2M: Every 2 Months; Q12M: Every 12 Months; Q4M: Every 4 Months; RT-qPCR: Reverse Transcription-Quantitative Polymerase Chain Reaction; 3L: Third Line; Data source *:KOLs' Input, Greek Treatment Protocol for Chronic Myeloid Leukemia; **KOLs' Input

RESULTS

- A total of 132 CML-CP prevalent cases in ≥3L treatment were estimated, receiving one of the available TKIs in Greece, including bosutinib, dasatinib, nilotinib and ponatinib.
- The estimated annual total cost for all ≥3L CML-CP patients (N = 132) in Greece was €5,324,800.
- Drug acquisition costs were the key cost driver, accounting for 96.1% of the total cost, followed by monitoring costs (3.8%), and hospitalization costs (0.1%) among ≥3L CML-CP patients **(Figure 1)**.

RESULTS (Continued)

Figure 1. Annual total cost allocation for ≥3L CML-CP patients



- Among costs incurred for managing AEs, a similar trend was observed with drug acquisition cost being the main cost driver among ≥3L CML-CP patients.
- In terms of disease monitoring, the costs of disease specific and AE related laboratory and image tests were the top contributors to the total monitoring cost **(Table 2)**.

Table 2. Annual total cost allocation for ≥3L CML-CP patients

Cost-of-illness of CML-CP	Annual Costs
Drug acquisition costs	**€5,116,699**
Disease specific treatment	€5,113,653
Adverse events treatment	€3,046
Monitoring costs	**€204,216**
Laboratory and Imaging tests	**€192,194**
Laboratory and Imaging tests - disease specific	€160,975
Laboratory and Imaging tests for AEs	€31,219
Physician visits	**€12,022**
Physician visits disease specific	€6,563
Physician visits for AEs	€5,459
Hospitalizations	**€3,884**
Hospitalization due to AEs	€3,884
Total	**€5,324,800**

Abbreviations: AEs: Adverse Events; 3L CML-CP: Third Line-Chronic Myeloid Leukemia-Chronic Phase; €: Euro

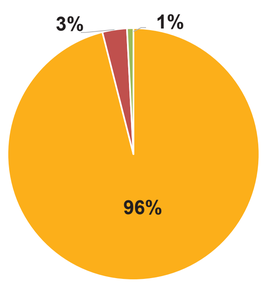
- A sub-analysis of annual total cost highlighted a higher proportion of costs for drug acquisition and disease monitoring resources (disease-specific treatment) than the costs associated with AEs **(Figure 2)**.

Figure 2. Sub-analysis of annual total cost allocation for ≥3L CML-CP patients

Total cost: €5,324,800

- Drug acquisition costs (only disease-specific treatment) **€5,113,653**
- Monitoring costs (only disease-specific treatment) **€167,538**
- Adverse events* **€43,609**

*Summation of AEs treatment, laboratory and imaging tests for AEs, physician visits for AEs, hospitalization due to AEs, which are available in Table 2.



- The estimated total annual cost per CML-CP patient undergoing ≥3L treatment for a 1-year treatment period was €40,236. The key cost driver was the drug acquisition cost, which was estimated at €38,663, accounting for 96,1% of the total cost. Monitoring cost was the second largest component (€1,543), followed by hospitalization costs (€29).

Limitations

- This study exclusively examined direct medical costs, excluding direct non-medical costs (transportation costs to and from the hospital, home/family care) and indirect costs (productivity loss). Hence, to provide a more comprehensive picture of overall cost estimates in future, evaluation of non-medical direct costs and indirect costs would be essential.
- This analysis is based on the estimated ≥3L CML-CP prevalent cases in Greece, derived from the international publications and confirmed by KOLs, indicating the lack of national published epidemiological data.

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Disclosures

Christiana Tychala, Panos Stafylas, Angeliki Avgitidou are employees of HealThink. Dimou Maria has received honoraria and consulting fees from Novartis Hellas. Nikolaos Charchalakis has received Honoraria from Astra Zeneca, AbbVie και Novartis. Repousis Panagiotis has received honoraria and consulting fees from Novartis Hellas. Antonopoulou Vasiliki is employee at Novartis Hellas

References

1. Jabbour E et al. *Am J Hematol.* 2018 Mar;93(3):442-459. **2.** Hochhaus A, et al. *Leukemia.* 2020 Apr;34(4):966-984. **3.** Bower H, et al. *J Clin Oncol.* 2016 Aug 20;34(24):2851-7. **4.** Sasaki K, et al. *Lancet Haematol.* 2015 May;2(5):e186-93. **5.** Breccia M, et al. *Adv Ther.* 2023 Mar;40(3):961-974. **6.** Hochhaus A, et al. *Leukemia.* 2020 Jun;34(6):1495-1502. **7.** McGarry LJ, et al. *Curr Med Res Opin.* 2016;32(2):289-99. **8.** Dimopoulos A-M, et al. Therapeutic protocol for Chronic Myeloid Leukemia; *General Secretariat of the Ministry of Health, Ministry of Health Greece*; 2018. **9.** NCCN. NCCN Clinical Practice Guidelines in Oncology: Chronic Myeloid Leukemia: National Comprehensive Cancer Network, Inc.; 2022. **10.** Hochhaus A et al. *Annals of oncology.* 2017;28(suppl_4):iv41-iv51. **11.** Baccarani M et al. *Blood.* 2013;122(6):872-84. **12.** Eurostat. Population on 1st January by age, sex and type of projection, online data code: PROJ_19NP, last update: 09/02/2021. 2021. **13.** National Cancer Institute: Cancer Stat Facts: Leukemia-Chronic Myeloid Leukemia (CML), 2019. **14.** Delord M et al, *Leukemia Research.* 2018 Jun 1;69:94-9. **15.** Canadian Cancer Society: Prognosis and survival for chronic myelogenous leukemia.