Operational and Economic Impact of CLL Treatment Regimens: Insights From a Multidisciplinary Study in Portugal

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Introduction

B-cell **chronic lymphocytic leukaemia** (CLL), with an annual incidence of 0.42 per 10,000 people, is the **most frequent type of leukaemia among European adults**.[1,2]

Although direct medical expenses (such as drug costs and hospital stays) are relatively well documented, the hidden costs associated with treatment administration and patient support are often overlooked. These include the time required for medication preparation, the use of hospital resources such as day hospital chair occupancy, transportation, patient education, and management of treatment-related adverse events (AEs). Understanding these costs is essential for optimizing resource allocation and improving the efficiency of patient care.

Objectives

- To identify and quantify additional non-medical direct costs associated with the treatment of CLL patients.
- To assess healthcare professionals' (HCPs) workload related to medication preparation, patient management, and AE handling.
- To assess the burden on patient by measuring time spent in hospital settings, including appointments, day hospital visits, and pharmacy dispensing.
- To compare the operational and economical impact of different therapeutic regimens.

Methods

Individual semi-structured interviews were conducted with 6 HCPs (**2 physicians, 2 nurses, and 2 pharmacists**) **from 4 different Portuguese public hospitals**. **Information on treatment strategies employed for CLL, time allocated by each healthcare professional, resource consumption, and time spent by patients** was collected. The interviews' findings were validated in a group workshop with 5 out of 6 of the same interviewees. From the consolidated data, **a comprehensive analysis was conducted for a one-year time horizon**.

Costs were assessed from the **perspective of public hospitals within the Portuguese NHS**, using the Euro (€) as the reference currency. **Day hospital occupation unit cost** was given by published complementary diagnostic (MCDT) codes 65001 (for <1-hour administrations), 65002 (1- to 3-hour administrations), and 65003 (>3-hour administrations), multiplied by a factor of €5.20. **HCPs-related costs** were based on the average salaries per working hour from the Public Administration Remuneration System for 2025, multiplied by the respective time allocated. **Appointment costs** were given by Portaria nº 207/2017. **Consumable unit costs** were based on public contracts (using base.gov.pt) or directly provided by HCPs.

Comparisons were drawn between oral, subcutaneous (SC), and intravenous (IV) regimens (Figures 4, 5, and 6), with each regimen considering the average times/costs of the treatment strategies that compose them: "Oral" includes Acalabrutinib/Ibrutinib (counted as only one treatment strategy) and Ibrutinib+Venetoclax; "SC" includes Rituximab+Ibrutinib, Rituximab+Idelalisib, and Rituximab+Venetoclax; "IV" includes Rituximab+Ibrutinib, Rituximab+Idelalisib, Rituximab+Venetoclax, Obinutuzumab+Venetoclax, and Fludarabine+Cyclophosphamide+Rituximab (FCR).

Results

Figure 1 | Time allocated by each healthcare professional (+ day hospital occupation time)

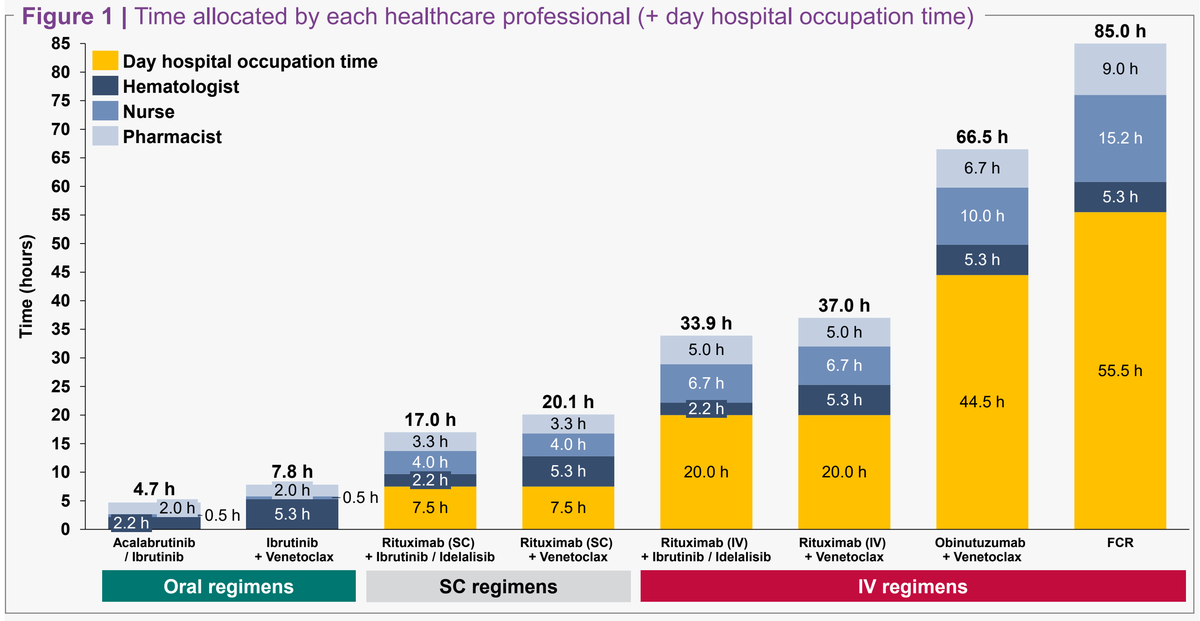


Figure 2 | Cost per patient, by cost category

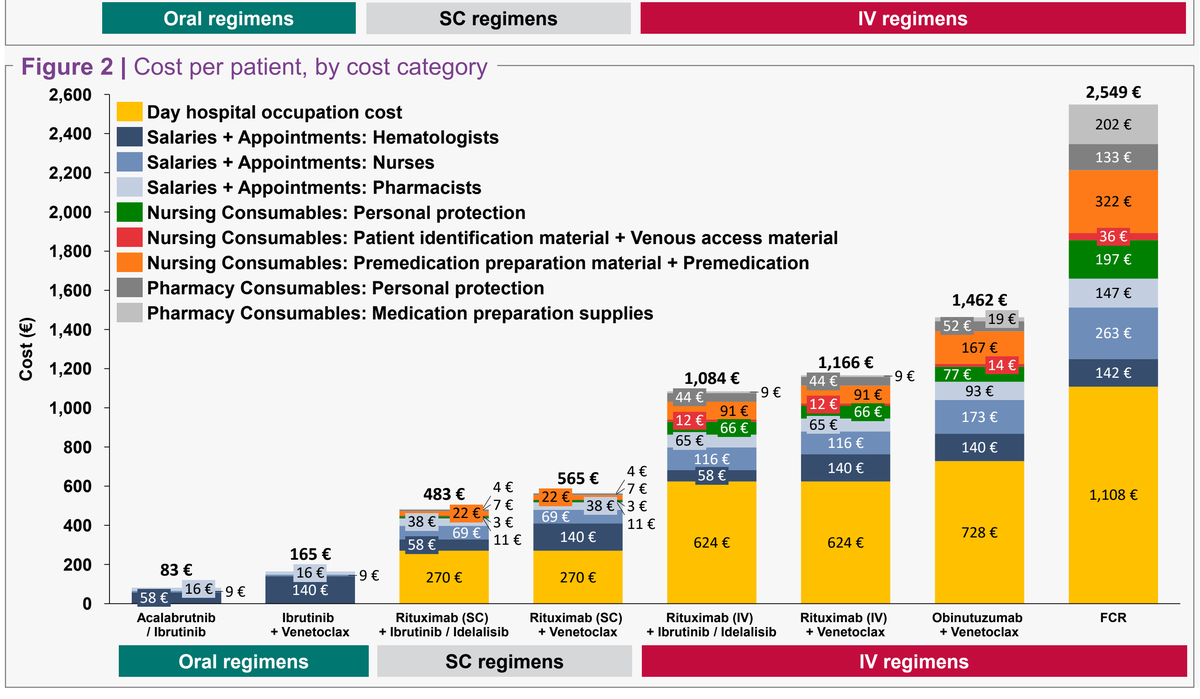


Figure 3 | Time spent by patients, by category

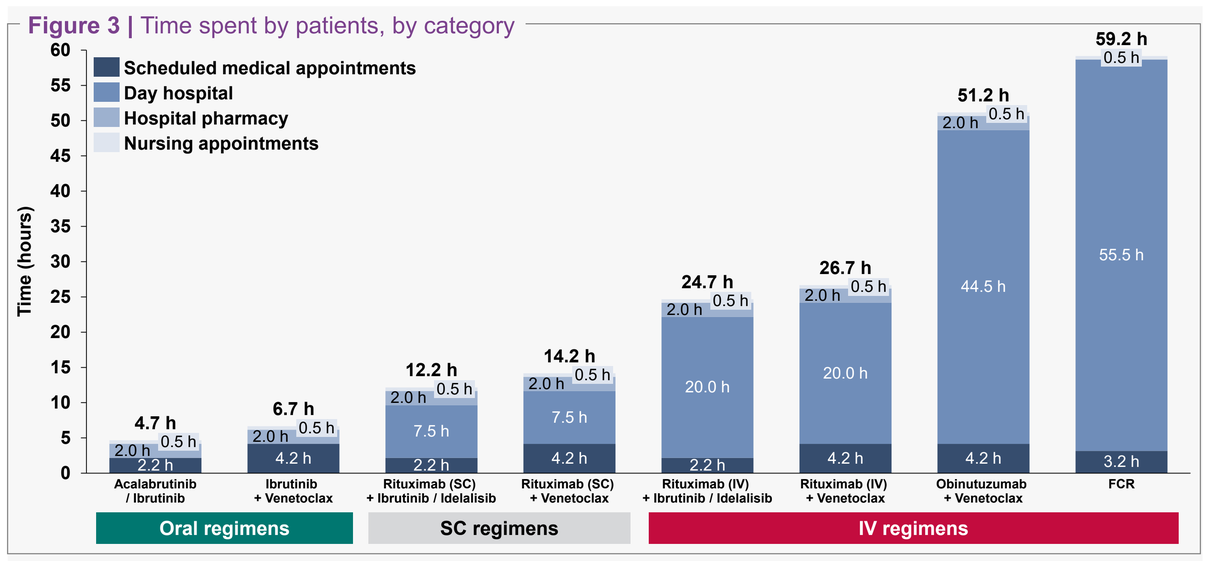


Figure 4 | Total time allocated by professionals by administration route

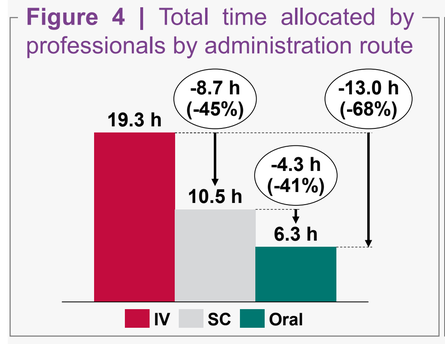


Figure 5 | Total costs by administration route

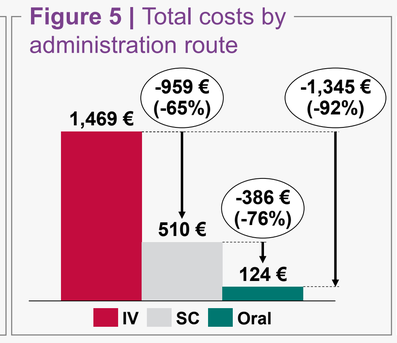
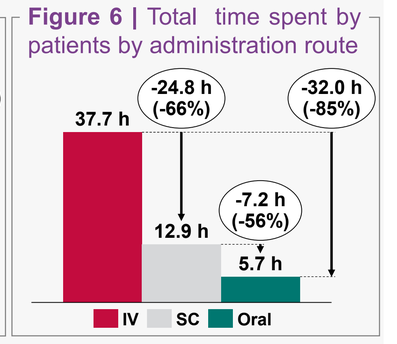


Figure 6 | Total time spent by patients by administration route



Since some centres treat CLL patients who live far from the hospital, IV treatments can have a significant impact on patients' lives, as an entire day may be lost to travel (e.g. 4 hours for patients from Bragança who are treated in Porto), treatment itself, laboratory tests, and waiting times (around 7 hours).

Adverse event management

- Patients receiving Venetoclax who are elderly (higher hydration needs), have lymphocytosis, or high tumour burden (thus at higher risk of tumour lysis syndrome), are typically hospitalized for 48 hours with each dose escalation; about 5% require this additional care.
- HCPs have the perception that most patients experience infusion-related reactions during the first Obinutuzumab administration. These reactions often require slowing the infusion rate and administering corticosteroids and antihistamines. Sometimes, patients may need to receive adrenaline and (more rarely) might need to be transferred to the emergency department.
- Unscheduled visits may consume about 3 hours in total (approximately 30 minutes for initial medical assessment, 15 minutes for vitals and sampling, 2 hours waiting for laboratory results, and 30 minutes for re-assessment/education).
- Fewer than 5% of patients are hospitalized due to AEs.
- Neutropenia-related infections are the most frequent reason for hospitalization.

Potential improvements

Potential improvements were also discussed, and the following feedback was collected:

- Medication dispensing at community pharmacies or at home.
- Online platform (potentially based on artificial intelligence) with the ability to automatically assist/triage patients who are reporting AEs.
- Proactive phone call from physicians/nurses during the peak drug action (when AEs are most likely to occur), to evaluate if the patient has any complaints.

Limitations

- The qualitative design of the study may introduce subjectivity and variability.
- Given the small sample size of HCPs and Hospitals, findings should be interpreted with caution when considering wider generalization.

Take-home messages

When considering a 1-year horizon, oral regimens, compared to IV and SC regimens, reduce treatment time and costs for each patient in the following magnitude:

	Oral vs. IV	Oral vs. SC
Nurses' time allocation	-8.6 hours (-94%)	-3.5 hours (-88%)
Pharmacists' time allocation	-4.1 hours (-67%)	-1.3 hours (-39%)
HCPs' overall time allocation	-13.0 hours (-68%)	-4.3 hours (-41%)
Overall costs	-1,345 € (-92%)	-386 € (-76%)
Patients' time spent	-32.0 hours (-85%)	-7.2 hours (-56%)

When considering a 1-year time horizon and focusing exclusively on newly approved first-line finite regimens (Ibrutinib + Venetoclax), compared to Obinutuzumab + Venetoclax, reduce treatment time and costs for each patient in the following magnitude:

	Ibrutinib + Venetoclax vs. Obinutuzumab + Venetoclax
Nurses' time allocation	-9.5 hours (-95%)
Pharmacists' time allocation	-4.7 hours (-70%)
HCPs' overall time allocation	-14.2 hours (-65%)
Overall costs	-1,297 € (-89%)
Patients' time spent	-44.5 hours (-87%)

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