do 17p, realizado em 18 pacientes (18%), apresentando del17p em 4 pacientes (22%). A pesquisa de hipermutação somática do IgHV, realizada em 9 pacientes, revelou IgHV não mutado em 6. Setenta e sete pacientes haviam recebido tratamento específico durante o seguimento. A causa da morte foi relacionada a LLC em 53 pacientes. Nestes pacientes, as mais frequentes foram: infecção em 41 (77%) casos (sendo COVID em 4 -10%), progressão de doença em 9 (17%) (ex: anemia hemolítica autoimune refratária, síndrome de Richter, Leucemia Mieloide Aguda pós tratamento e restrição a transfusão por motivo religioso), cardiovascular em 2 (4%) e causa desconhecida em 1 (2%). Trinta e um pacientes (58%) estavam recebendo tratamento no momento do óbito (94% com quimioimunoterapia e 6% com ibrutinibe). Nos 47 casos em que o motivo do falecimento não teve relação com a LLC, as principais causas foram: infecção em 36 (75%) casos (a maioria por pneumonia, sendo 11 casos com COVID), segunda malignidade em 3 (6%), eventos cardiovasculares em 5 (11%) e causas desconhecidas em 4 (8%). **Conclusão:** Trata-se de um grupo de pacientes, que apesar de apresentar idade mediana abaixo de outras casuísticas de pacientes com LLC da literatura, apresenta alta incidência de comorbidades e performance status inferior (refletidos pelo ECOG e CIRS).A principal causa de óbito tanto relacionada como não relacionada a LLC foi infecção, o que aponta para a necessidade de melhor manejo dessas complicações e do uso de terapias com menor risco de levar ao desenvolvimento das mesmas.

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CONCOMITANT USE OF VENETOCLAX 100 MG AND KETOCONAZOLE TO TREAT CLL IN A PUBLIC CENTER IN BRAZIL

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Introduction: Venetoclax has demonstrated substantial efficacy in the treatment of chronic lymphocytic leukemia (CLL). However, the metabolism of venetoclax primarily relies on the cytochrome P450 enzyme CYP3A4, which can be influenced by concurrent administration of strong CYP3A4 inhibitors (ex: ketoconazole). These drugs have the potential to interact with venetoclax by inhibiting its metabolism resulting in elevated venetoclax plasma concentrations. Venetoclax availability in the public setting in Brazil is currently limited, with irregular donations being the only possible source. Therefore, we have made the decision to utilize ketoconazole to save venetoclax tablets in an effort to maximize treatment opportunities for as many patients as possible. **Objective:** Evaluate the efficacy and safety of the combination therapy of ketoconazole, low-dose venetoclax, and rituximab in the treatment of patients with CLL. **Methods:** Patients received venetoclax starting on day 22 of cycle 1, with a 5-week dose ramp-up (20 mg, 50 mg, 100 mg, and 200 mg). Subsequently, they received venetoclax 100 mg in combination with ketoconazole 200 mg daily until completion of cycle 12 (for patients in the first line of treatment) or cycle 24 (for patients in further treatment lines). Intravenous rituximab was also administered for six cycles, 375 mg/m^2 in cycle 1 and 500 mg/m^2 in cycles 2 to 6. All patients included in the analysis had received a minimum of 6 months of treatment at the time of data collection. **Results:** A total of 21 treatment regimens for 18 patients were included in this analysis. The median duration of venetoclax treatment was 12 months, ranging from 6 to 24 months. Six patients (29%) received the treatment as a first-line therapy, 5 (24%) as a second-line therapy, 8 (38%) as a third-line therapy, and the remaining patients received it in further lines of treatment. The overall response rate was 100%, with 14 treatments leading to a complete response and 7 treatments to a partial response. Among the partial responders, 4 patients are still receiving treatment, and 2 patients completed six months of treatment and were referred to an allogeneic stem cell transplantation. The most common grade 3 or 4 adverse event observed was neutropenia, which occurred in 12 treatments. Notably, no cases of grade 2 or higher hepatic toxicity related to ketoconazole were reported. Additionally, there were no treatment-related deaths observed in the study. At a median follow-up of 19 months (range: 6-33), the median progression-free survival (PFS) has not been reached, and the PFS at 24 months was 83%. Three cases of disease progression occurred after 26, 30, and 39 months of treatment. All three patients were successfully retreated with the same treatment combination and achieved at least a partial response again. The median overall survival (OS) has not been reached, and the OS at 24 months was 95%. Three deaths were recorded during the study period: one patient died from acute myelogenous leukemia, one patient from a myocardial infarction, and one patient due to an unrelated intestinal bleeding. **Discussion and conclusion:** Our data indicate that the combination of ketoconazole, low-dose venetoclax, and rituximab showed favorable tolerability and promising effectiveness in patients with CLL. Further studies are warranted to confirm these observations and validate the potential benefits of this combination regimen in the management of CLL in similar settings.

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RESULTS OF CONSERVATIVE INDICATION CRITERIA FOR FIRST-LINE TREATMENT IN CHRONIC LYMPHOCYTIC LEUKEMIA: INSIGHTS FROM THE BRAZILIAN REGISTRY OF CLL

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Introduction: Chronic lymphocytic leukemia (CLL) exhibits diverse treatment requirements, with some patients receiving immediate treatment while others remain under observation. In 2008, the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) established criteria for treatment indications, widely adopted in clinical practice and trials. The Brazilian Group of CLL (BGCLL) has been evaluating a more conservative approach to treatment indication performed in multiple centers, which avoids predefined cutoff levels for cytopenias and refrains from considering progressive lymphocytosis, extranodal involvement, or disease-related symptoms as isolated criteria. However, the safety and potential different outcomes of this conservative approach compared to the strict IWCLL criteria remain uncertain. Objective: This study aims to compare the outcomes of CLL patients without indication for treatment according to the BGCLL criteria, who were either treated or not based on the center's decision. **Methods:** We conducted a retrospective analysis of CLL patients enrolled in the Brazilian Registry of CLL, observed between January 2009 and July 2023, meeting the minimum data availability criteria for analysis and following IWCLL inclusion guidelines. **Results:** A total of 2412 patients from 43 centers were included. Among them, 1326 patients (55%) met the IWCLL criteria for treatment indication, while only 558 patients (23%) fulfilled the more conservative BGCLL indication. Of the 1254 untreated patients, 50 (20%) had a treatment indication based on IWCLL guidelines. Common indications for treatment initiation included cytopenias in 160 patients (64%), disease-related constitutional symptoms in 43 patients (17%), and symptomatic lymphadenopathy in 22 patients (9%). Non-treatment despite having an indication was attributed to BGCLL's more conservative criteria in 67% of cases, severe comorbidities in 6%, and death during follow-up in 27%. Among the 1158 treated patients, 93 patients (8%) received treatment despite lacking a treatment indication according to the IWCLL criteria. According to BGCLL's conservative criteria, 602 (52%) treated patients did not have a treatment indication. After a median follow-up of 58 months (range: 3-506), the overall survival (OS) was 70% at 8 years. Among patients without an indication for treatment according to BGCLL's conservative criteria, OS was significantly worse in treated patients (79%) compared to untreated patients (64%, $p < 0.0001$, figure 1). **Conclusion:** These real-world data demonstrate that a conservative approach in indicating first-line treatment for CLL is safe and associated with improved survival, possibly by mitigating toxicities and treatment-related complications such as clonal selection. Furthermore, this strategy may conserve resources, enhancing drug accessibility for a larger number of patients in clear need of treatment, particularly in low-income countries.

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FRAILTY ASSESSMENT AS PREDICTOR OF BLEEDING FOR PATIENTS TREATED WITH ACALABRUTINIB

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Introduction: The American Society of Clinical Oncology (ASCO) promotes the routine use of a comprehensive geriatric assessment, particularly emphasizing frailty, to identify vulnerabilities not detected in the standard clinical evaluation. However, frailty remains an under-explored topic in Chronic Lymphocytic Leukemia (CLL), especially concerning modern treatments such as Bruton's tyrosine kinase inhibitors (BTKi). There's a paucity of data linking this assessment to treatment toxicity. Objective: To document the clinical progression of CLL patients undergoing Acalabrutinib treatment and correlate toxicity with a frailty assessment protocol. Methodology: Patients treated with Acalabrutinib underwent a specific geriatric assessment protocol. For frailty assessment, the modified Fried frailty criteria and the Frail Scale were employed. The Lawton scale was used to gauge functionality in instrumental activities of daily living (IADL), and sarcopenia was assessed in accordance with the updated guidelines from the European Working Group on Sarcopenia. **Results:** Two patients were clinically categorized as frail and one as robust. Patient J.R.M, a 95-year-old female without significant comorbidities, was classified as frail, sarcopenic, and dependent for IADLs. She commenced treatment with Acalabrutinib, but after nine days, experienced severe skin bleeding leading to drug discontinuation. The second patient, M.N.G.O, a 78-year-old hypertensive female, was also identified as frail, sarcopenic, with IADL impairment. After initiating Acalabrutinib therapy, she developed skin and muscular bleeding shortly after, prompting immediate cessation. The last patient, R.S.M, a 91-year-old male with well-managed multiple comorbidities, was categorized as robust and non-sarcopenic. He has been on Acalabrutinib treatment for CLL for 1 year and 7 months, displaying a positive therapeutic response, no side effects, and full independence in IADLs. Discussion: Acalabrutinib is a second generation BTKi, safer than Ibrutinib. Its use has been suggested as safe in any age group. Still, data in frail patients is scarce. The German CLL study group provided safety data on Acalabrutinib in elderly patients but did not