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Introduction: Ibrutinib, a Bruton's tyrosine kinase (BTK) inhibitor, is associated with increased survival and prolonged response, even in high-risk scenarios, with relatively low toxicity compared to chemoimmunotherapy. However, a significant number of patients discontinue therapy due to intolerance and toxicity. It is essential to comprehend the factors contributing to discontinuation and the subsequent impact on outcomes. **Objective:** This analysis aims to utilize real-world data to assess ibrutinib's effectiveness and to examine factors contributing to discontinuation and the subsequent impact on clinical outcomes in Brazil. **Methods:** All patients who received ibrutinib as continuous monotherapy at any therapy line between January 2015 and March 2024, with essential minimum data on patient and treatment characteristics, clinical outcomes, and a minimum follow-up of three months, were included. **Results/Discussion:** A total of 278 patients from 29 centers were included. Ibrutinib was used in the first line of treatment (LoT) in 23%, second LoT in 42%, third line in 21%, and fourth or subsequent lines in 14%. The majority were male (63%), with a median age of 68 years (range: 35-95), and most (44%) had significant comorbidities. TP53 mutation or del(17p) status was assessed in 173 patients (62%), with 38 (22%) testing positive. The median duration of ibrutinib treatment was 28 months (range: 6 days - 103 months). The median interval between diagnosis and initiation of ibrutinib was 53 months (range: 0-330), shorter for those in 1st or 2nd lines (40 months) than later lines (89 months). Ibrutinib was discontinued in 51% of cases, primarily due to toxicity (32%), death (29%), disease progression (26%), and other factors (13%). In several cases, ibrutinib was replaced by another BTK inhibitor by the physician's preference A significant proportion (51%) experienced at least one treatment-related toxicity. Patients in the first or second line had fewer adverse events than those in later lines (46% vs. 59%, $p = 0.04$). Common toxicities included infections (28%), bleeding (11%), hematologic toxicity (9%), cardiac toxicity (5%), and diarrhea (4%). Atrial fibrillation occurred in 5% of cases. Median PFS was not reached. After a median follow-up of 50 months (range: 3-105), PFS was 64% at 4 years. PFS was significantly shorter in patients who received ibrutinib in later lines (48% vs. 72% in first or second lines, $p < 0.0001$), and in those with del(17p)/TP53 mutations compared to those without (50% vs. 69%, $p = 0.008$). The median time-to-next-treatment (TTNT) was 56 months: 17 months for patients who used ibrutinib for less than 2 years, 47 months for 2-4 years, and 84 months for more than 4 years. Overall survival (OS) at 4 years was 70%, shorter for patients in later lines (57% vs. 77% for 1st or 2nd lines, $p = 0.006$). The most common causes of death were infections in 63% of cases (on ibrutinib in 45%, and after stopping ibrutinib in 18%), disease progression (18%), and cardiac complications (7%). **Conclusions:** Ibrutinib shows favorable effectiveness in Brazilian CLL patients across all treatment lines. Intolerance and discontinuation were relatively common, affecting treatment effectiveness, especially in patients receiving ibrutinib late in the disease course, possibly related to cumulative adverse events from previous lines.

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RECORRÊNCIA DE AMILOIDOSE EM ÓRGÃO SÓLIDO APÓS TRANSPLANTE CARDÍACO: UMA REVISÃO SISTEMÁTICA

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Introdução: Na amiloidose sistêmica há o acúmulo de fibrilas amiloides em diversos tecidos e órgãos, incluindo o coração. Dentre os 30 tipos de proteínas amiloidogênicas descritos, 5 acometem este órgão: cadeias pesadas e leve da imunoglobulina, transtirretina, amiloide A e apoA1. A amiloidose cardíaca é uma cardiomiopatia restritiva com disfunção ventricular e diminuição da hipertrofia cardiovascular devido a alterações no sistema de condução decorrentes da deposição das cadeias amiloides, sendo uma importante indicação de transplante cardíaco (TC). Pela dificuldade em encontrar doadores e acometimento de múltiplos órgãos, a possibilidade de recorrência da doença após o TC deve ser ponderada. **Objetivos:** Avaliar a recorrência de amiloidose em pacientes após TC. **Métodos:** Trata-se de revisão sistemática de literatura, na qual foram selecionados artigos por meio de busca eletrônica nas bases de dados PubMed, Lilacs, Cochrane e Scielo. Os descritores foram "Recurrence", "Cardiac amyloidosis" e "Heart transplant" e 74 artigos foram identificados. A busca incluiu artigos em português e inglês publicados desde 1988 até 2023. Durante a fase de revisão, aplicação dos critérios de inclusão e avaliação crítica, foram selecionados 11 artigos. **Resultados:** O TC, junto a regimes quimioterápicos e ao transplante de células tronco hematopoiéticas (TCTH), é uma modalidade possível para o tratamento da amiloidose cardíaca, porém não é o método mais preferível, devido ao risco de recorrência da doença no aloenxerto. Embora tenham sido relatados casos de recidiva neste órgão sólido, detectou-se aumento da sobrevida global de pacientes submetidos ao TC quando comparados a pacientes não transplantados e que o risco de tal complicação não demonstra ser relevante a curto e médio prazo. A remissão hematológica da doença também foi constatada a partir do TCTH e de tratamentos quimioterápicos prévios e posteriores ao TC. **Conclusão:** Apesar da recorrência de amiloidose em pacientes após TC, essa terapêutica continua a ser utilizada pela gravidade progressiva

do quadro e pelo correlato aumento de sobrevida após o procedimento. É fundamental a realização de pesquisas para o desenvolvimento de tratamentos alternativos e mecanismos de identificação precoce do quadro, bem como mais estudos com amostras maiores, para entender melhor o perfil dos pacientes acometidos por essa condição e assim caracterizar melhor o curso da doença.

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ANALYSIS OF CLINICAL OUTCOMES OF THE CONSERVATIVE APPROACH IN TREATMENT INDICATIONS IN CHRONIC LYMPHOCYTIC LEUKEMIA: INSIGHTS FROM THE BRAZILIAN REGISTRY OF CLL

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Introduction: In 2008, the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) established criteria for treatment indications. The Brazilian CLL Group (GBLLC) has been evaluating a more conservative approach in the indication and initiation of treatment carried out in multiple centers. This approach eschews predefined cut-off levels for cytopenias and refrains from considering progressive lymphocytosis, extranodal involvement, or disease-related symptoms as isolated criteria. However, the safety and potential divergent outcomes of this conservative strategy in comparison to the more stringent IWCLL criteria had not yet been tested. **Objective:** To compare the outcomes of patients with CLL registered in the Brazilian CLL Registry (RBLLC) without indication of treatment according to the GBLLC criteria, who were treated or not based on the center's decision. **Patients and Methods:** We performed a retrospective analysis of patients with CLL registered in the RBLLC who were followed between January 2009 and July 2023, meeting the minimum data availability criteria for analysis and following the IWCLL inclusion guidelines. **Results/Discussion:** A total of 2,511 patients from 41 centers were included. Among them, 1,404 patients (56%) met the treatment indication criteria set by IWCLL, while only 788 patients (31%) met the more conservative criteria established by GBLLC. Predominant indications for treatment initiation in the IWCLL indication group included cytopenias in 771 patients (55%), symptomatic lymphadenopathy in 330 patients (24%), and disease-related constitutional symptoms in 112 patients (8%). In the GBLLC indication group, common indications for treatment initiation comprised cytopenias in 413 patients (52%), symptomatic lymphadenopathy in 316 patients (40%), and autoimmune complications in 22 patients (3%). After a median follow-up of 58 months, the 5-year overall survival (OS) was 82%. The group of patients whose treatment indication were cytopenias demonstrated inferior OS compared to those with other indications. Of the total of 1,404 patients who had an indication according to the IWCLL, 1,149 received therapy. Median time to first treatment (TTT1) was 3.4 months (range: 1 – 231). Upon evaluating the duration between the treatment indication and its initiation, patients who waited over 18 months exhibited a superior OS in contrast to those with a waiting period of fewer than 18 months (82% vs. 69%, respectively; $p = 0.004$). Among patients with treatment indication according to IWCLL but without indication according to the GBLLC criteria, OS was significantly worse in treated patients (83%) as compared with untreated patients (97%, $P < 0.0001$). After multivariate analysis, receiving treatment was an independent risk factor for OS in patients with indication according to the IWCLL and but not to the GBLLC criteria. **Conclusion:** These real-world data suggest that a conservative approach to first-line treatment for CLL is not only safe but also linked to enhanced survival, potentially by reducing treatment-related toxicities and complications, such as infections, toxicities and clonal selection. Additionally, this strategy holds the potential to save resources improving access to medications for a larger pool of patients with a clear need for treatment, particularly in resource-limited countries.

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RELATO DE CASO: LEUCEMIA LINFOCÍTICA CRÔNICA ATÍPICA EM UMA APRESENTACAO RARA POR LESAO LITICA MEDULAR

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Introdução: A Leucemia Linfocítica Crônica (LLC) é a leucemia mais comum em adultos, caracterizada pela proliferação de linfócitos B maduros, principalmente homens idosos. A suspeita clínica é levantada diante de linfocitose no sangue, adenomegalias e complicações autoimunes. **Objetivo:** Relatar o caso de um paciente do sexo masculino, internado em julho de 2023 no Hospital Municipal Dr. Moyses Deutsch-SP (HMMD), com dor lombar crônica e adenomegalia, secundário a Leucemia Linfocítica Crônica Atípica (LLCa). **Metodologia:** Relato de caso, um estudo observacional retrospectivo de