[b] Hospital de Transplantes Euryclides de Jesus Zerbini - Hospital Brigadeiro, São Paulo, Brazil
[c] Division of Hematology, Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil
[d] Instituto do Câncer do Estado de São Paulo (ICESP), Faculdade de Medicina da Universidade de São Paulo (FMUSP), São Paulo, Brazil
[e] Instituto Hemomed de Oncologia e Hematologia, São Paulo, Brazil
[f] Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, Brazil
[g] Hospital Israelita Albert Einstein (HIAE), São Paulo, Brazil
[h] Irmandade da Santa Casa de Misericórdia de São Paulo (ISCMSP), São Paulo, Brazil
[i] Hospital Nove de Julho, São Paulo, Brazil

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.

https://doi.org/10.1016/j.htct.2023.09.386

FRAILTY ASSESSMENT AS PREDICTOR OF BLEEDING FOR PATIENTS TREATED WITH ACALABRUTINIB

TX Carneiro [a,b,c], JLS Sales [a], JS Tavares [a], IJM Wanderley [a], JKD Santos [a], LBC Leão [b,c], LDS Pimentel [b], NS Moraes [a]

[a] Universidade do Estado do Pará (UEPA), Belém, Brazil
[b] Hospital Ophir Loyola (HOL), Belém, Brazil
[c] Hospital Porto Dias Mater Dei, Belém, Brazil

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

specifically detail the adverse effects in patients meeting the criteria for frailty syndrome. Conclusion: The presented cases suggest that geriatric assessment may be a more accurate predictor of adverse events in BTKi treatment than chronological age. Thiago Xavier Carneiro receives honoraria from Janssen.

https://doi.org/10.1016/j.htct.2023.09.387

FRAILTY ASSESSMENT IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA TREATED WITH THE COMBINATION OF VENETOCLAX AND IBRUTINIB

TX Carneiro [a,b,c], JLS Sales [a], JS Tavares [a], IJM Wanderley [a], JKD Santos [a], LDS Pimentel [b], NS Moraes [a]

[a] *Universidade do Estado do Pará (UEPA), Belém, Brazil*
[b] *Hospital Ophir Loyola (HOL), Belém, Brazil*
[c] *Hospital Porto Dias Mater Dei, Belém, Brazil*

Introduction: The American Society of Clinical Oncology (ASCO) advocates for the routine use of a comprehensive geriatric assessment, emphasizing frailty, to pinpoint vulnerabilities that might go unnoticed in standard clinical evaluations. Currently, limited information is available on the optimal management of toxicity in patients treated with the combination of new agents for Chronic Lymphocytic Leukemia (CLL). Objective: To delineate the geriatric assessment of a CLL patient who underwent treatment with a combination of Venetoclax and Ibrutinib. Methodology: The patient in question followed a service-specific geriatric assessment protocol. Frailty was assessed using the modified Fried frailty criteria and the Frail Scale. Instrumental Activities of Daily Living (IADL) functionality was gauged using the Lawton scale, while sarcopenia was evaluated in line with the updated guidelines from the European Working Group on Sarcopenia. **Results:** R. S.A., a 74-year-old male with no notable comorbidities, was referred in 2019 due to the discovery of 6 cm intra-abdominal lymph nodes on a CT scan. An axillary lymph node biopsy confirmed a lymphocytic lymphoma diagnosis. His complete blood count was within the normal range. He was under observation until the end of 2020 when he began to show symptoms and had enlarged retroperitoneal lymph nodes measuring 9.3 cm, along with increased cervical, supraclavicular, axillary, and mediastinal lymph nodes. The IgVH mutation test was inconclusive, and the 17p deletion was not detected. Ibrutinib therapy was initiated in January 2021 with a dosage of 140 mg administered three times daily. The patient saw a generalized reduction in lymphadenopathy after 9 months. A Positron Emission Tomography (PET) scan in January 2023 revealed 2.5 cm abdominal lymph nodes, with the patient being asymptomatic. He expressed an interest in limited-duration therapy and had a detectable residual disease at 1% in the peripheral blood. Before the combined therapy, the geriatric assessment rated him as robust, independent for IADLs, and with no motor function impairments. Venetoclax therapy commenced in January 2023. The patient progressed without symptoms of tumor lysis or any other adverse symptoms after 6 months of combined therapy. Discussion: The combined therapy of Ibrutinib and Venetoclax, which has recently gained approval, was researched in elderly patients or those with comorbidities in the GLOW study. This study exclusively utilized age over 65 and comorbidities as predictors of toxicity (CIRS). Significant adverse effects were reported, with 69% of patients experiencing grade 3/4 adverse events. We postulate that, in the described case, the geriatric assessment could identify a patient who, despite advanced chronological age, was able to tolerate the treatment without dose reductions or adverse events. Conclusion: The geriatric assessment holds promise as a predictive tool for toxicity in the combined therapy of Ibrutinib and Venetoclax for CLL. Thiago Xavier Carneiro receives honoraria from Janssen.

https://doi.org/10.1016/j.htct.2023.09.388

LEUCEMIA MIELOIDE CRÔNICA E OUTRAS SÍNDROMES MIELOPROLIFERATIVAS CRÔNICAS INCLUINDO AS POLICITEMIAS

INIBIDORES DE AURORA QUINASES EXIBEM ATIVIDADE ANTINEOPLÁSICA EM CÉLULAS BA/F3 CSF3RT618I

NS Parducci [a], ADMB Garnique [a], K Lima [a,b], JAEG Carlos [a], NP Fonseca [c,d], LBL Miranda [a], EM Rego [b], F Traina [c,d], JA Machad-Neto [b]

[a] *Departamento de Farmacologia, Instituto de Ciências Biomédicas, Universidade de São Paulo (USP), São Paulo, SP, Brasil*
[b] *Laboratório de Investigação Médica em Patogênese e Terapia Dirigida em Onco-Imuno-Hematologia (LIM-31), Departamento de Clínica Médica, Divisão de Hematologia, Faculdade de Medicina, Universidade de São Paulo (HCFMUSP), São Paulo, SP, Brasil*
[c] *Departamento de Imagem Médica, Hematologia e Oncologia, Faculdade de Medicina de Ribeirão Preto (FMRP), Universidade de São Paulo (USP), Ribeirão Preto, SP, Brasil*
[d] *Centro de Terapia Celular, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Ribeirão Preto, SP, Brasil*

Objetivos: As neoplasias mieloproliferativas (NMP) se consolidam como um grupo relevante de doenças derivadas do mau funcionamento do processo de hematopoese e têm por atributo particular a proliferação aumentada de uma ou mais séries mieloides. Dentre estas, distinguem-se as leucemias neutrofílicas crônicas (LNC), causadas pela mutação T618I do gene *CSF3R*, traço que gera a ativação do receptor independente de ligante e a sinalização *downstream* através da via JAK2/STAT. Estudos anteriores em linhagem linfocítica dependente de IL3, Ba/F3, demonstraram que mutações em BCR::ABL1 e $JAK2^{V617F}$ aumentaram a expressão de proteínas da família da aurora quinase (AURKs), mais especificamente de AURKA e de AURKB. Estudos pré-clínicos têm ilustrado a