Introdução: A mastocitose sistêmica (MS) é uma doença hematológica rara e complexa, muitas vezes subdiagnosticada devido à sua apresentação clínica heterogênea e aos desafios que impõe ao diagnóstico preciso. Caracteriza-se pelo acúmulo anormal de mastócitos em diversos órgãos e tecidos, o que pode levar a uma série de sintomas e complicações. Por ser uma condição com múltiplas formas e manifestações, cada caso representa um verdadeiro quebra-cabeça clínico para os médicos. **Descrição do caso:** O relato clinico é de um homem, 71 anos, com história de etilismo importante que interna devido hemorragia digestiva alta (HDA) por varizes de esôfago, ascite e esplenomegalia, recebendo diagnóstico de hepatopatia crônica. Além do quadro gastrointestinal apresentava eosinofilia persistente (picos >20.000/μL), anemia normocítica (Hb 8.8 g/dL) e plaquetopenia (73.000/μL). A investigação hematológica teve início com o aspirado de medula óssea: hipercelular com eosinofilia, todas as fases maturativas, com ausência de parasitas e excesso de blastos. Imunofenotipagem de MO apresentava 3,3% de mastócitos atípicos com expressão aberrante de CD25 e CD2, cariótipo diploide, biópsia de MO hipercelular com eosinofilia (65%), agregados densos de mastócitos atípicos >15 por campo e fibrose grau 3; com perfil imunohistoquímico dos mastócitos com expressão de CD2 e CD30, além da triptase sérica >200 ng/mL. Clinicamente sem manifestações alérgicas, mas com osteoporose grave e fratura patológica de fêmur esquerdo. No nosso serviço não disponibilizamos dos testes moleculares PDGFA e CKIT, por isso não foram realizados. Dessa forma, considerando os dados dos mastócitos apresentados e o perfil medular proliferativo com eosinofilia persistente o melhor diagnóstico para o paciente, segundo a Organização Mundial da Saúde (OMS), é a Neoplasia hematológica eosinofílica associada a Mastocitose Sisêmica (MS-NHA) com achados C de hepatopatia. O tratamento inicial instituído foi imatinibe 100 mg/dia com remissão parcial da eosinofilia, a dose foi aumentada para 400 mg/dia com a confirmação da MS. Além de associação de ácido zoledrônico de 5 mg/ano e suplemento de cálcio, para controle ósseo. No entanto o paciente apresentou nova HDA e faleceu em decorrência ao sangramento gastrointestinal. O diagnóstico de MS-NHA é sempre um desafio pela raridade dos casos e as múltiplas possibilidades diagnósticas, mesmo com todos as definições descritas recentemente (U, Celalettin e colaboradores publicada em 2025) e na 5ª edição da Classificação de Tumores Hematolinfoides da OMS: Neoplasias Mieloides e Histiocíticas/Dendríticas, o diagnóstico de MS-NHA foi lento e só foi possível por meio da integração entre achados morfológicos, imunofenotípicos e clínicos. A ausência dos testes moleculares nos hospitais públicos do SUS dificulta e prolonga o tempo do diagnóstico preciso e a definição terapêutica. **Conclusão:** Esse caso ilustra como, mesmo diante de recursos moleculares limitados nos hospitais públicos brasileiros, é possível reconhecer formas avançadas da MS, desde que se mantenha alto grau de suspeição clínica. Por isso os hematologistas, alergistas, gastroenterologistas, endocrinologistas, dermatologistas e patologistas devem estar atentos a esse diagnóstico.

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DIFFERENT ADHERENCE RATES TO TYROSINE KINASE INHIBITORS AND THEIR RELATION TO CLINICAL OUTCOMES IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA: PRELIMINARY RESULTS FROM A SYSTEMATIC REVIEW

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Introduction: Ensuring adherence to Tyrosine Kinase Inhibitors (TKI) therapy is crucial for Chronic Myeloid Leukemia's (CML) treatment success. Vigilant monitoring allows early detection of treatment failures enabling prompt medication adjustments. This underscores a major challenge in managing TKI therapy for CML patients, given that the minimum adherence rate required for maintaining a satisfactory response remains unclear. **Objectives:** Thus, this systematic review aims to answer the question: what is the minimal adherence rate needed for patients with BCR::ABL1 positive CML undergoing TKI therapy to achieve a satisfactory molecular response? **Material and methods:** Therefore, a systematic review is being conducted following the PRISMA guideline and Cochrane Handbook. The protocol was registered on PROSPERO (CRD42024558338). The research question, eligibility criteria, and search strategy were established using the PICOS acronym. The search strategies were applied on PubMed (MEDLINE), Scopus, Embase, Web of Science, and Cochrane Central Register of Controlled Trials. The publication date was restricted to 1998 and later, as the first clinical trial investigating TKI therapy in CML was initiated from that year onward. The initial search was conducted on 24 May 2024 and will be updated prior to the narrative synthesis. The study selection was performed through blinded peer review using Rayyan QCRI®. A third reviewer (a topic expertise) solved the discrepancies. At this time, three independent reviewers are conducting the data extraction using a standard Excel® table and, after that, the expertises will validate the data extracted. The risk of bias and overall quality of evidence will be evaluated after data extraction. A narrative synthesis of the findings will be provided. A meta-analysis will be conducted if a minimum of three comparable studies is found. **Discussion and conclusion:** A total of 10,054 records were identified. After removal of duplicates, 6,595 records remained for title and abstract screening. 114 studies were selected for full-text screening. Of these, four were unavailable. Ultimately, 32 studies met the eligibility criteria and were included for data extraction. Until now 25 studies were extracted. Observational studies were the leading study design. The most frequent adherence measurement methods were pill count, variations of the Morisky Medication Adherence Scale questionnaire, Medication Event Monitoring System, and Medication Possession Ratio. Most studies enrolled patients in the chronic phase. The main criteria for the

evaluation of clinical outcomes was the European Leukemia Net Guidelines. Countries were diverse, including nations across different income strata. So far, studies have indicated that adherence is strongly associated with better major molecular response, complete cytogenetic response and event-free survival, being higher adherence rates (≥ 85%) consistently linked to superior clinical outcomes. Adverse effects and treatment intolerance were commonly reported as key contributors to non-adherence, leading patients to discontinuation. At the end of this study, it is expected to establish a clear threshold for adherence to TKI therapy that correlates with a satisfactory molecular response in patients with CML, ultimately enhancing monitoring strategies to improve patient outcomes.

Reference:

Jabbour E, Kantarjian H. Chronic myeloid leukemia: 2025 update on diagnosis, therapy, and monitoring. Am J Hematol. 2024;99:2191–212. doi: 10.1002/ajh.27344.

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DIFFERENTIALLY EXPRESSED PROTEINS IN PLASMA-DERIVED EXTRACELLULAR VESICLES FROM CHRONIC MYELOID LEUKEMIA PATIENTS

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Introduction: CML is a myeloproliferative neoplasm driven by the BCR::ABL1 fusion gene. Resistance to TKIs, especially in cases with the T315I mutation, remains a major challenge. Plasma EVs are stable carriers of molecular information and potential biomarkers for monitoring CML and resistance mechanisms. **Objectives:** To identify differentially expressed proteins in EVs from healthy individuals and CML patients grouped by treatment response and T315I mutation status, aiming to discover biomarkers of resistance and poor response. **Material and methods:** EVs were isolated from plasma of healthy controls and five CML patient groups. Proteomic analysis was performed using mass spectrometry, followed by statistical and functional pathway analyses to identify proteins linked to resistance and disease progression. **Results:** Proteomic profiling revealed distinct protein expression patterns across the patient groups. Notably, several proteins involved in cytoskeletal organization (ACTN1, FLNA, MYH9, TUBA1B, TUBB4B, VIM), histones (H3F3B, HIST1H2AJ, HIST1H4A), molecular chaperones (HSP90AB1), and other regulatory proteins (LGALS3BP, CKB) were significantly downregulated in EVs from PTR compared to HC, GTR, TFR and/or T315I patients in different contexts. The chaperone protein HSP90AB1, which intracellularly has been implicated in oncoprotein stabilization and therapy resistance, was found at lower levels in EVs from PTR, indicating a complex role of EV-associated HSP90AB1 distinct from intracellular mechanisms. Additionally, SSC5D, a protein less studied in CML, emerged as a potential specific biomarker for the T315I mutant group (found upregulated in T315I compared to PTR, GTR, TFR and P-315I), suggesting a unique EV signature associated with this resistant mutation. Functional enrichment highlighted alterations in cytoskeleton remodeling, immune response, and apoptotic pathways linked to the differentially expressed proteins. **Discussion and conclusion:** Our study reveals distinct proteomic signatures in plasma extracellular vesicles (EVs) from chronic myeloid leukemia (CML) patients, linked to treatment response and mutation status. EVs from poor treatment responders (PTR) showed downregulation of key cytoskeletal proteins (e.g., ACTN1, FLNA, MYH9), histones, and immune-related molecules (LGALS3BP), suggesting altered vesicle biogenesis and intercellular communication in resistant cells. Notably, HSP90AB1 was reduced in PTR EVs despite its known intracellular increase in resistance, highlighting differences between intracellular and EV protein profiles. Additionally, SSC5D emerged as a potential biomarker for T315I-mutated patients, offering a non-invasive mutation marker. These findings support the use of EV proteomics as a tool for monitoring CML progression and resistance, with implications for personalized therapy. Proteomic analysis of plasma extracellular vesicles reveals candidate biomarkers related to poor treatment response and T315I mutation in chronic myeloid leukemia. The distinct EV protein signatures identified offer promising tools for patient stratification and monitoring, advancing precision medicine approaches in CML management. Further studies are warranted to validate these biomarkers and elucidate their functional roles in leukemogenesis and resistance mechanisms.

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EFEITO CITOESTÁTICO DO LÁTEX DE *EUPHORBIA UMBELLATA* NA LINHAGEM DE LEUCEMIA MIELOIDE CRÔNICA K562

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Introdução: A Leucemia Mieloide Crônica (LMC) é uma neoplasia mieloproliferativa clonal e rara, de evolução lenta e progressiva, caracterizada pela produção excessiva de leucócitos anormais. A utilização empírica de plantas