

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 ($\geq 85\%$) 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:

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<https://doi.org/10.1016/j.htct.2025.104419>

ID - 1178

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.

<https://doi.org/10.1016/j.htct.2025.104420>

ID - 2861

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