Objective: Myeloproliferative neoplasms (MPNs) are clonal disorders characterized by activation of JAK/STAT and related pathways, leading to excessive proliferation, resistance to apoptosis and inflammation. The JAK2 inhibitor Ruxolitinib (Ruxo) is indicated for some groups of patients with MPN, reducing symptoms and improving overall survival. However, the factors that influence its effectiveness in reducing malignant clones and, consequently, the emergence of resistance, are not fully understood. Besides, the Focal Adhesion Kinase (FAK), a kinase involved in adhesion, migration, proliferation and apoptosis, participates in JAK2 V617F-positive cells'viability and apoptosis, and Ruxo seems to modulate genes related to the Focal Adhesion pathway in a public RNAseq dataset of SET-2 cells, as previously shown by this research group. The present work aimed to investigate whether the Focal Adhesion pathway is modulated after Ruxo treatment in JAK2 V617F-positive cells HEL cells, by analyzing two publicly available RNAseq datasets. **Materials and methods:** GSE184850 and GSE229712 were selected for analysis from the "Gene Expression Omnibus" (www.ncbi.nlm.nih.gov/geo/). Both datasets are from RNAseq in HEL cells (JAK2 V617F-positive) treated with DMSO and Ruxo 0.5 uM for 48h. The datasets were first analyzed separately for differentially expressed genes (DEGs) using DESeq2 package in R and Rstudio. Then, the common DEGs among top 250 DEGs were determined using ggVennDiagram package and analyzed in the STRING database (string-db.org) for KEGG pathways enrichment. **Results:** There were 153 common DEGs. Enrichment analysis in STRING database showed that Focal Adhesion pathway was among the 10 KEGG relevant pathways, with 10 DEGs: *RELN, SHC1, ITGA5, IGFR1, FLT4, VASP, CCDN2, ACTN1, KDR, ZYX* (strength 0.82, FDR: 0.00060). *RELN* and *IGF1R* were upregulated in Ruxo compared to DMSO, in both datasets, while *SHC1, ITGA5, FLT4, VASP, CCDN2, ACTN1, KDR, ZYX* were downregulated. **Discussion:** The downregulated genes are directly involved in migration and invasion processes. They are associated with cytoskeleton remodeling, which is important for disease progression. In addition, their expression is dysregulated in other types of cancers and leukemias. Upregulated genes *RELN* and *IGF1R* are genes involved in the activation of signaling pathways related to disease progression, such as those associated with proliferation and survival. **Conclusions:** The present results indicate a possible modulation of Focal Adhesion pathway after Ruxo treatment, which may be involved in treatment effectiveness and, therefore, further investigations regarding involvement of these genes in MPN may contribute to elucidate the influence of this pathway on patient treatment and prognosis.

https://doi.org/10.1016/j.htct.2024.09.833

EFFICACY OF OLVEREMBATINIB IN THE TREATMENT OF REFRACTORY CHRONIC MYELOID LEUKEMIA: A SYSTEMATIC REVIEW AND SINGLE-ARM META-ANALYSIS

CLL Furtado [a], GFM Filho [b], MLMR Costa [c], LAMPL Lugo [a], RM Delgado [b], GCTB Neto [c], PHF Grisi [d], GC Lira [c]

[a] *Universidade Federal da Paraíba (UFPB), João Pessoa, Brazil*
[b] *Universidade Federal de Campina Grande (UFCG), Campina Grande, Brazil*
[c] *Faculdade de Medicina Nova Esperança (FAMENE), João Pessoa, Brazil*
[d] *Centro Universitário UNIFACISA, Campina Grande, Brazil*

Objective: To perform a systematic review and meta-analysis to evaluate the efficacy of Olverembatinib, a novel BCR::ABL1 tyrosine kinase inhibitor (TKI), in refractory chronic myeloid leukemia (CML). **Material and methods:** PubMed, Embase and Cochrane database were searched, until June 2024, for randomized clinical trials (RCTs) that assess the efficacy of Olverembatinib in patients with CML, with or without *T315I* mutation, who have failed at least two prior TKI therapy. The primary outcomes were Major Molecular Response (MMR), Complete Cytogenetic Response (CCyR) and Major Cytogenetic Response (MCyR). Statistical analysis was performed using R-4.4.1. Heterogeneity was examined with I^2 statistics. **Results:** 238 patients were included from 3 RCTs, with follow-up ranging from 0 to 5 years. The pooled analysis revealed an MMR of 0,4205 (95% CI [0,2789 - 0,5765]; $p < 0,01$); a CCyR of 0,5501 (95% CI [0,3529 - 0,7328]; $p < 0,01$) and an MCyR of 0,6548 (95% CI [0,4886 - 0,7902]. Heterogeneity was high across all outcomes, with I^2 values of 85% for MMR, 88% for CCyR and 85% for MCyR. **Discussion:** The results demonstrate that Olverembatinib has significant efficacy in achieving high rates of MMR, CCyR and MCyR in refractory CML patients. However, the high heterogeneity observed in all three outcomes suggests notable variability across studies. This variability likely stems from differences in baseline characteristics, including the number of prior TKI treatment lines and median treatment duration among study populations. The small number of studies included also contributes to this variability. **Conclusion:** Olverembatinib shows promise as an effective treatment option for refractory CML. However, further research is warranted to elucidate the significant heterogeneity observed across studies, optimize treatment strategies, and provide more robust evidence of its efficacy.

https://doi.org/10.1016/j.htct.2024.09.834

MASTOCITOSE SISTÊMICA COM MUTAÇÃO C-KIT EXON 17 (D816V): RELATO DE CASO

FF Camargo, ET Saito, ABD Manduca, JA Gomes, LQ Marques, DSC Filho, FM Marques, MDS Pastori, DAG Eguez, LLM Perobelli

Hospital de Transplantes Euryclides de Jesus Zerbini - Hospital Brigadeiro, São Paulo, SP, Brasil

Introdução: A mastocitose é uma doença rara com uma incidência de 1 em 10.000 pessoas e predominância em mulheres adultas. Ela se caracteriza pelo acúmulo anormal de mastócitos, que podem se limitar à pele (mastocitose cutânea) ou afetar outros tecidos (mastocitose sistêmica). Os sintomas incluem máculas na pele, rubor, taquicardia, diarreia, anafilaxias e pancitopenias. O diagnóstico de mastocitose sistêmica segue os critérios da OMS de 2016, que incluem infiltração densa de mastócitos em órgãos e medula óssea