15) e KMT2A-WT (n = 392). Foi encontrado 631 genes superexpressos e 1318 baixo expressos e determinamos os 10 genes mais diferencialmente expressos (SMAD9, RNF220, CPEB2, SUPT3H, SLC38A11, MYO6, PDCD6IPP1, PRELID3BP7, PDCD6IPP2, C1QTNF7- AS1). Em seguida, definimos a diferença de expressão entre os grupos, ambos os genes SKIDA1 (p = 1.7e-9) e LAMP5 (p = 0.0084) foram significativamente superexpressos no grupo KMT2A-r em comparação com KMT2A-WT e não foi observada diferença de expressão significativa em CSPG4 (p = 0.96). Além disso, avaliamos a performance dos biomarcadores e foi observado que SKIDA1 (AUC: 0.959) e LAMP5 (AUC: 0.719) performaram melhor que CSPG4 (AUC: 0.480). Ainda, os valores preditivos (VPP, VPN) foram calculados para cada biomarcador respectivamente, SKIDA1 (0.074; 1), LAMP5 (0.064; 0.99) e CSPG4 (0.035; 0.96). **Discussão e conclusão:** Os resultados preliminares obtidos a partir da série de casos do TARGET sugerem que LAMP5 e SKIDA1 apresentam desempenho promissor na predição de rearranjos em KMT2A, possivelmente superando o biomarcador tradicional CSPG4. A análise de expressão diferencial, associada à avaliação por curvas ROC e métricas preditivas, reforça o potencial desses genes como marcadores diagnósticos. No entanto, a validação definitiva requer a análise da série de casos do laboratório, que está em andamento, para confirmar a robustez e a aplicabilidade clínica desses achados.

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VENETOCLAX COMBINED WITH INTENSIVE CHEMOTHERAPY REGIMENS FOR PATIENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA. A SYSTEMATIC REVIEW AND SINGLE-ARM META- ANALYSIS

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Introduction: Following the demonstrated success of the BCL-2 inhibitor venetoclax in combination with hypomethylating agents for newly diagnosed acute myeloid leukemia (AML), its potential role in the difficult-to-treat relapsed/refractory AML (R/R AML) population has become an important area of investigation. **Objectives:** This systematic review and meta-analysis aim to evaluate the efficacy and safety of venetoclax when combined with intensive chemotherapy regimens for patients with R/R AML. **Material and methods:** A systematic literature search was conducted across the PubMed, Embase, and Cochrane Central databases from their inception through February 2025, aimed to identify randomized controlled trials (RCTs) and observational studies that evaluated the efficacy and safety of venetoclax in combination with intensive chemotherapy regimens for patients with R/R AML. The primary outcomes of interest included complete remission rate (CR), overall response rate (ORR), and composite complete remission rate (CRc). Secondary outcomes focused on therapy-related adverse events. Response criteria were assessed according to the European Leukemia Network (ELN) guidelines for AML. Subgroup analyses were performed based on the specific intensive chemotherapy combinations used. Statistical analysis was performed using RStudio (version 4.4.2). Heterogeneity among studies was evaluated using random-effects models and assessed by the I2 statistic. **Discussion and conclusion:** The analysis included six non-RCTs retrospective studies, comprising a total of 235 patients. Two studies utilized a fludarabine, filgrastim, and idarubicin (FLAG-VIDA, n = 79) regimen; Two studies employed a fludarabine, idarubicin, and venetoclax (FLAVIDA, n = 87) regimen; Two studies used a combination of cladribine, low-dose cytarabine, and venetoclax (CAV, n = 69). The sample sizes of the individual studies ranged from 18 to 61 patients. The median age across the studies ranged from 40 to 65 years. Cytogenetic profiles were reported as adverse in 124 patients (52%). For the pooled data across all studies, the CRc was 51.45% (95% CI: 36.15−66.76; p < 0.01; I2= 83.5%). The ORR was 63.79% (95% CI: 49.67−77.92; p < 0.01; I2= 82.0%). The pooled CR rate among five studies (n = 185) was 27% (95% CI: 9.18−57.50; p < 0.01; I2= 84.6%). Due to the divergence in intensive chemotherapy regimens, a subgroup analysis was conducted. The CRc rates were as follows: FLAG-VIDA: 66.03% (95% CI: 55.62−76.45; p = 0.4; I2= 0%); FLA-VIDA: 59.77% (95% CI: 49.47−70.07; p = 0.9; I2= 0%); and CAV: 27.52% (95% CI: 16.99−38.06; p = 0.8; I2= 0%). The ORR for each subgroup were: FLAG-VIDA: 70.1% (95% CI: 60.06−80.14; p = 0.3581; I2= 0%); FLA-VIDA: 69.25% (95% CI: 51.24−87.26; p < 0.0578; I2= 72.2%); and CAV: 32.8% (95% CI: 11.75−88.63; p < 0.04; I2= 91.9%). Pooled analysis of adverse events revealed that the incidence of febrile neutropenia was 71.38% (95% CI: 31.65−100; p < 0.01; I2= 95.6%). The incidence of pneumonia was 23.6% (95% CI: 16.8−32.08; p = 0.6; I2 = 0%). Conclusion: Our study findings support that venetoclax combined with intensive chemotherapy can achieve meaningful hematologic responses in patients with R/R AML and may serve as a bridge to transplant in eligible patients. Subgroup analysis showed that the FLAG- VIDA/FLA-VIDA regimens outperformed the CAV regimen. However, further prospective RCTs are needed to confirm these results and define the optimal role of this combination therapy.

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VENETOCLAX COMO TERAPIA DE RESGATE PARA LEUCEMIA MIELOIDE AGUDA RECIDIVADA/REFRATÁRIA: EVIDÊNCIA DE MUNDO REAL NO BRASIL

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