Venetoclax-based combinations for acute myeloid leukemia: optimizing their use in Latin-America

Combinaciones basadas en venetoclax para la leucemia mieloide aguda: optimizando su uso en América Latina

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ABSTRACTO: Objectives: Venetoclax combinations are a new standard for patients with acute myeloid leukemia (AML). We aimed to evaluate the safety and efficacy of these combinations in a period of accelerated approval in Latin-America.Methods: This observational study evaluated adults with acute myeloid leukemia who received venetoclax-based therapy in 11 public or private centers in Mexico and Peru for both newly diagnosed or relapsed and refractory AML.Results: Fifty patients were included; 28 with newly diagnosed (ND) AML and 22 with relapsed/refractory (RR) disease. ND patients were older (64 vs. 40 years; $p < 0.001$) with a lower functional capacity (ECOG ≥2 64.3% vs 9%; $p < 0.001$). Venetoclax was frequently combined with azacytidine (60%) and prophylactic azoles (82%) with a median maximum dose of 200 mg (range, 100-600 mg). Hematologic toxicities were common. Complete response rates including patients with incomplete hematopoietic recovery were 78.6% in ND and 45.5% in RR patients, with a median overall survival of 9.6 (95% CI 3.7-15.5) and 8 months (95% CI 4.8-11.2).Discussion: Our study showed a preferred use of venetoclax plus azacytidine over cyatrabine. Patients in the first-line setting were similar to those in the landmark studies, while most patients with relapsed disease had received prior intensive therapies. Responses were favorable, with a median survival in agreement to other reports, albeit shorter than that observed in the randomized phase-3 trials.Conclusion: Venetoclax-based therapy in AML was effective despite dose reductions and prophylactic antifungals in two middle-income countries outside of a clinical trial setting.

Identification and Targeting of the Developmental Blockade in Extranodal Natural Killer/T-cell Lymphoma

Identificación y focalización del bloqueo del desarrollo en el linfoma de células T/asesinas naturales extraganglionares

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ABSTRACTO: Extranodal natural killer/T-cell lymphoma (ENKTL) is an aggressive, rare lymphoma of natural killer (NK) cell origin with poor clinical outcomes. Here we used phenotypic and molecular profiling, including epigenetic analyses, to investigate how ENKTL ontogeny relates to normal NK-cell development. We demonstrate that neoplastic NK cells are stably, but reversibly, arrested at earlier stages of NK-cell maturation. Genes downregulated in the most epigenetic immature tumors were associated with polycomb silencing along with genomic gain and overexpression of EZH2. ENKTL cells exhibited genome-wide DNA hypermethylation. Tumor-specific DNA methylation gains were associated with polycomb-marked regions, involving extensive gene silencing and loss of transcription factor binding. To investigate therapeutic targeting, we treated novel patient-derived xenograft (PDX) models of ENKTL with the