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615.ACUTE MYELOID LEUKEMIAS: COMMERCIALLY AVAILABLE THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Efficacy and Safety Analysis of Venetoclax Combined with Azacitidine in Real-World Treatment of Patients with AML

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Objective: To evaluate overall survival (OS), response rate, time to first response, duration of response, depth of response, and safety in real-world treatment with Venetoclax (Ven) combined with Azacitidine (AZA) in patients with Acute Myeloid Leukemia (AML).
Methods: From January 2019 to December 2021, 31 patients with AML who completed at least 2 courses of Ven (100-400mg, 28 days), the Ven dose was adjusted based on drug interactions particularly with azole antifungal prophylaxis, and AZA (75mg/m ^{2},7 days). Baseline characteristics: Median age 65 years (30-82 years), including 5 patients ≥75 years. ECOG score: 19 patients (61.3%) scored 0-1, 12 patients (38.7%) scored 2-3. Type of AML: 20 De novo cases (64.5%), 8 MDS or MPN conversion cases (25.8%), 3 primary AML-MRC cases (9.7%). Previous treatment: 22 patients (71%) were initially treated, 8 patients (25.8%) were relapsed/refractory, and 1 patient (3.2%) was maintained after remission with standard therapy. At baseline, grade 3 or greater cytopenia was associated: 3 cases were anemia (9.7%), 13 cases were neutropenia (41.9%), and 14 cases were thrombocytopenia (45.2%). Bone marrow original cell count: < 30% (10 cases), 30-50%(9 cases), ≥50% (12 cases). Cytogenetic risk: 1 case was low risk (3.2%), 19 cases were medium risk (61.3%), 10 cases were high risk (32.3%), and 1 case was no dividing phase (3.2%). Molecular mutations included: NRAS/KRAS mutation in 12 cases, DNMT3A mutation in 11 cases, NPM1 mutation in 9 cases, IDH1/2 mutation in 6 cases, FLT3-ITD mutation in 5 cases each, HOX11 positive, ASXL1, RUNX1 and NPM1+FLT3-ITD mutation in 3 cases each.
Results: After a median of 3 courses of treatment (C2-C15), 3 of the patients underwent bridge hematopoietic stem cell transplantation after remission. The best efficacy was evaluated in CR+CRi: 22 patients (71%), PR: 5 patients (3 of whom were refractory to recurrence), SD: 3 patients (1 of whom was refractory to recurrence), and NR: 1 patient (refractory to recurrence). First-line efficacy was better than second-line or multi-line. Median time to start treatment to reach CR/CRi: 45 days, DOR: 314 days. The negative response rate of flow MRD in CR/CRi patients was 81.8%, including 11 cases of C1 conversion, 3 cases of C2 conversion, 3 cases of C3 conversion and 1 case of C4 conversion. Flow minimal residual disease (MRD) persisted in AML1-ETO subgroup. The early combined response rate of patients with important gene mutations: ASXL1 and RUNX1 mutation subgroup 100%, NPM1 mutation subgroup 77.78%, IDH1/2 mutation subgroup 83.33%, FLT3-ITD mutation subgroup 80%, HOX11 positive subgroup 80%, 66.67% in the NPM1+FLT3-ITD and NRAS/KRAS mutation subgroups, 53.55% in the DNMT3A mutation subgroup, and 1 patient with TP53 mutation was not in remission. The median OS of the first-line/ maintenance treatment group was 19 months, which was better than the median OS of the second-line or multi-line treatment group was 7 months. Safety: The incidence of tumolysis syndrome and early treatment-related mortality was 0; The incidence of early reduction or treatment interruption was higher (25.8%). Severe adverse reactions included sepsis in 2 cases, severe pneumonia in 2 cases and septic shock in 1 case.
Conclusions: In the real world first-line treatment of high-risk AML patients with Ven combined with AZA, the disease control and survival were initially improved, and the early combined response rate (CR+CRi) of molecular subgroups IDH1/2, NPM1, RUNX1, ASXL1, FLT3-ITD and HOX11 were higher. The higher incidence of adverse events in early treatment and delayed treatment may be related to 41.9% of patients with grade 3 neutropenia at baseline, partly AML-MRC. So, based on Ven-28d/AZA, We still need to explore new therapeutic modalities which should balance the efficacy and safety.

Disclosures No relevant conflicts of interest to declare.

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