PB1813 EFFICACY OF AZACITIDINE AND VENETOCLAX IN AML PATIENTS MAY BE LIMITED BY INTERACTION WITH POSACONAZOLE AND LACK OF STANDARDISED TREATMENT PROTOCOL. REAL WORLD DATA FROM 3 MAJOR CENTRES IN SINGAPORE.

Topic: 04. Acute myeloid leukemia - Clinical

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Background:

Acute myeloid leukaemia (AML) is a disease of the elderly, with the median age at diagnosis being 68 years. However, both curative and palliative treatment options for elderly AML are limited, with dismal five-year survival outcomes. In Singapore, hypomethylating agents (HMA), particularly azacitidine, is the most used treatment in this cohort of patients. Consistent with results from the phase 3 trial, our experience with azacitidine only showed modest response at best, with complete response (CR) rate of 14.2% and median overall survival (OS) of 9.8 months.

Aims: Here, we report our experience with azacitidine and venetoclax in both newly diagnosed (ND) and relapsed/refractory (R/R) AML. We further evaluate the impact of heterogeneity in both patients and clinical practices on outcome with this novel treatment combination.

Methods:

We included 100 consecutive patients with ND and R/R AML, treated with azacitidine and venetoclax in three tertiary hospitals in Singapore from February 2017 to March 2020. These patients were deemed unfit for induction chemotherapy in view of their age/comorbidities. Azacitidine was dosed at 75mg/m² for seven days per cycle. The target dose of venetoclax was 400mg once a day. For those on concomitant strong CYP3A4 inhibitor, reduced doses were given at the physicians’ discretion. The treating physicians also decided on the timing of bone marrow assessment as well as dose interruptions and modifications for toxicities. Minimal residual disease (MRD) was assessed via multiparameter flow cytometry (MFC) with a sensitivity of 10⁻⁴.

Baseline demographics data, disease characteristics and treatment details were obtained from electronic health records of the respective hospitals, after obtaining IRB approval.

Results: In ND patients, the overall response rate (ORR) was 51.9%: 16.7% achieved complete response (CR), 27.8% CR with incomplete count recovery (CRi), and 7.4% morphologic leukaemia-free state (MLFS). Amongst responders, MRD was undetectable in 13 (46%) patients. The median time to best response was 1.8 months (1.1-3.5 months) and median DOR was 4.8 months. Red cell transfusion independence was achieved in 38.2% of patients, and platelet transfusion independence in 41.8%. Median OS for ND patients was 8.4 months (4.6 months -NR). Responders had significantly longer median OS than non-responders (20 vs 3.55 months, p=<0.001).

For R/R patients, the ORR was 48.8% with 11.1% achieving CR, 33.3% CRi, and 4.4% MLFS. 41.9% of the responders had undetectable MRD. The median time to best response was 1.8 months (1.6-2.1 months) and median DOR was 4.9 months. 38.1% achieved red cell transfusion independence and 38.1% was platelet transfusion independent. The median OS for R/R patients was 8.6 months (4.9 months – NR), with the median OS for responders being significantly longer than non-responders (NR vs 4.93 months, p=0.006).

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13 patients (Five ND and eight R/R) proceeded to allogeneic SCT following response to azacitidine and venetoclax. Five (38.4%) had undetectable MRD prior to proceeding to transplant. 11 are still alive and in remission.

**Summary/Conclusion:**

In summary, our analysis demonstrated that azacitidine and venetoclax show high response rates and improved OS amongst patients who responded to treatment. However, survival and haematological improvement may be hampered by early discount intuition due to interaction with posaconazole and lack of adherence or availability of a standardised dose modification protocol. Alternative treatment strategies such as continuation of azacitidine as a single agent should also be explored.