ELSEVIER

Blood 142 (2023) 5934–5935

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

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

Ultra-Low-Dose of Decitabine with Venetoclax As Induction and Consolidation Therapy for Elderly or Frail Newly Diagnosed Acute Myeloid Leukemia and High Risk Myelodysplastic Syndrome Patients

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Background: Venetoclax with hypomethylating agents is a new standard of care for newly diagnosed (ND) patients with acute myeloid leukemia (AML) who are 75 years or older, or unfit for intensive chemotherapy. Pharmacodynamic studies have suggested superiority of the longer 10-day regimen of decitabine which has shown promising results in high-risk AML in phase 2 trials. We hypothesized that venetoclax with 10-day decitabine may be effective in ND and secondly AML/MDS, particularly for high-risk subgroups.

Methods: We retrospectively analyzed 45 patients with ND AML, secondary AML (sAML), or high-risk MDS who was older than 60 years or unfit for intensive chemotherapy due to frail / due to the COVID-19 pandemic. Patients were required adequate end-organ function. Patients received decitabine (6mg/m2 IV for 10-days) with oral venetoclax (400mg daily for 3 weeks (D10+VEN)) for induction, followed by the same chemo-free regimen for consolidation if patients responsed to induction therapy. The primary efficacy endpoint was overall response rate (ORR). The second endpoint was overall survival (OS) and progress free survival (PFS).

Findings: Between January, 2020 and July , 2023, 45 patients were treated with this regimen, 31 (68.9%) had ND AML, 8 patients (17.8%) had untreated sAML, 6 patients (13.3%) had untreated high-risk MDS. The median age was 65 years (IQR, 59-69) and 26(57.8%) patients had ECOG performance status of 3 or higher. The ORR among all patients was 82.2% and in disease subgroups were: ND AML, 87.1% (27/31) (95% CI 79, 94); untreated sAML, 75% (6/8); untreated high-risk MDS, 66.7%(4/6). According 2022 ELN risk classification by genetics, the ORR in favorable risk patients was 87.5%(7/8), intermediate risk patients was 100%(12/12), adverse risk patients was 72%(18/25). The most common treatment-emergent adverse events included infections with grade 3/4 neutropenia (n=36, 80%) and febrile neutropenia (n=7, 15.6%). There were 2 grade 5 adverse events including one infections with Enterobacter cloacae Bacteremias combined with heart failure because of the shortage of Blood product transfusion during the COVID-19 pandemic, and one case of intracranial hemorrhage related to prolonged grade 3/4 thrombocytopenia. The one year OS of all patients was 71.9%(23/32), and in favorable risk patients was 83.3% (5/6), intermediate risk patients was 72.7%(8/11), adverse risk patients was 73.3%(11/15). The two-year OS of all patients was 58.3%(7/12).

Conclusion: Ultra-low-dose of ten-day decitabine with venetoclax as induction and consolidation chemo-free therapy in elderly or frail newly diagnosed acute myeloid leukemia and high risk myelodysplastic syndrome result in high overall response rate and high 1-year overall survivial.

Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-191155