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POSTER ABSTRACTS

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

Venetoclax Plus Azacitadine for Middle Aged and Elderly Patients with Newly Diagnosed Acute Myeloid Leukemia: Interim Analysis of a Prospective, Multicenter, Single-Arm, Phase 2 Trial

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Background: "7+3" induction is the standard regimen in newly diagnosed young patients (pts) with acute myeloid leukemia (AML) fit for intensive chemotherapy with 60-80% complete remission rate. However, middle aged and elderly pts may experience more severe complications during induction therapy and overall survival is shorter than that of younger pts. Recently, venetoclax with azacitadine as induction therapy was approved as the first line therapy for pts with aged more than 75 years or unfit pts with composite complete remission (CRc) of 60-70%. We hypothesize that venetoclax with azacitadine as induction therapy in fit middle aged and elderly pts may have similar CRc rate and less complications. This study aims to evaluate the safety and efficacy of venetoclax plus azacitadine as induction therapy in fit middle aged and elderly newly diagnosed AML pts.

Methods:

This is an interim analysis of an ongoing phase 2 clinical trial (NCT05471700) of a planned 40 untreated AML pts aged 45-65 who were fit for intensive chemotherapy according to Ferrara Criteria. In cycle 1, pts received azacitadine 75mg/m2/day on d1-7 and venetoclax escalated from 100mg to 200mg to 400mg until 28-day cycle was finished. For pts with FLT3-ITD positive, sorafenib was optional administered at a dose of 400mg twice daily. Bone marrow assessments were performed on d28. Pts who achieved CRc (defined as complete remission[CR] and CR with incomplete hematologic recovery[CRi]) with intermediate or adverse risk groups received 1 or 2 cycles of consolidation with venetoclax plus azacitadine or center-specific cytarabine-based consolidation. Allogeneic stem cell transplantation (HSCT) was performed if a donor was available. Pts in favorable risk gruop received 3 to 4 cycles of center-specific intermediate or high dose cytarabine-base consolidation. Non-responders or pts who achieved partial remission received 1 more cycle of venetoclax plus azacitadine. Who could not get CRc after 2 cycles of induction would be withdrawn from the study. The primary objective is to determine the CRc rate. The secondary

objective is safety, MRD negative rate, duration of remission (DOR), the rate of allo-HSCT, event free survival (EFS), and overall survival (OS). The endpoint is to show that venetoclax plus azacitadine is not inferior to "3+7" induction in fit pts with newly diagnosed AML aged 45-65.

Results:

From 10/9/2022 to 6/30/2023, a total of 32 pts was enrolled to this study, comprising 18 males and 14 females. There were 27 (84%) pts with de novo AML, 2(6%) pts were secondary AML, 3 pts (9.4%) were therapy-related AML. Median age was 58 years (range, 45-64 years). There were 2(6%), 14(44%) and 16(50%) pts were in the favorable, intermediate and adverse risk group, respectively. The baseline patient characteristics are summarized in Table 1. Outcome data were updated as of June 30, 2023, for a median follow-up of 2.2(0.2-8.8) months. Among 27 evaluable pts, 21(77.8%) achieved CRc with 11(40.8%) in CR and 10(37.0%) in CRi, 2(7.4%) achieved PR in cycle1, while 23(85.2%) achieved CRc with 14(51.9%) in CR and 9(33.3%) in CRi, 4(14.8%) got induction failure after 2 cycles(Figure 1). A total of 16 (61.5%) pts got MRD negative among the pts with CRc after cycle1, and 17 (65.4%) after cycle2. CRc rate after 2 cycles in ELN2017 favorable, intermediate, adverse risk group was 100%, 83.3% and 85.0%, respectively, and MRD negative rate was 100%, 88.9% and 55.6%, respectively.

The regimen was well tolerated. No mortality occurred during induction therapy. The most common non-hematological grade 3/4 AE were febrile neutropenia (n=13, 40.6%),followed by pneumonia (n=3, 9.4%).Sepsis occurred in 1 (3.1%) pt. With a median follow-up of 2.2(0.2-8.8) months, the median remission duration, EFS and OS have not been reached.

Conclusions:

Preliminary results indicate that venetoclax plus azacitadine as an induction regimen for fit middle aged and elderly pts with newly diagnosed AML is promising with high CRc and low toxicity. Recruitment of adults with newly diagnosed aged 45-65 AML pts for this trial is ongoing.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Venetoclax was approved for patients with newly diagnosed AML older than 75 years or unfit for intensive chemotherapy. The present study is to evaluate the efficacy and safety of venetoclax plus azacitadine as indution therapy for middle aged and elder paients with newly diagnosed AML.

Table1 Baseline characteristics of patients

Subgroup	AZA+VEN (N=32)
Age, (years)	
Median(range)	58(45-64)
Sex, (%)	
Male	18(56.3)
Female	14(43.7)
WBC, (10^9/L)	
Median(range)	15.11(0.52-189.10)
Diagnosis, N (%)	
De novo AML	27(84.4)
Secondary AML	2(6.2)
Therapy-related AML	3(9.4)
Bone marrow blasts, N (%)	
< 50%	1(3.1)
≥30% to < 50%	7(21.9)
≥50%	24(75.0)
ELN 2017 risk group, N (%)	
Favorable	2(6.2)
Intermediate	14(43.8)
Adverse	16(50.0)

Figure1 Response rate

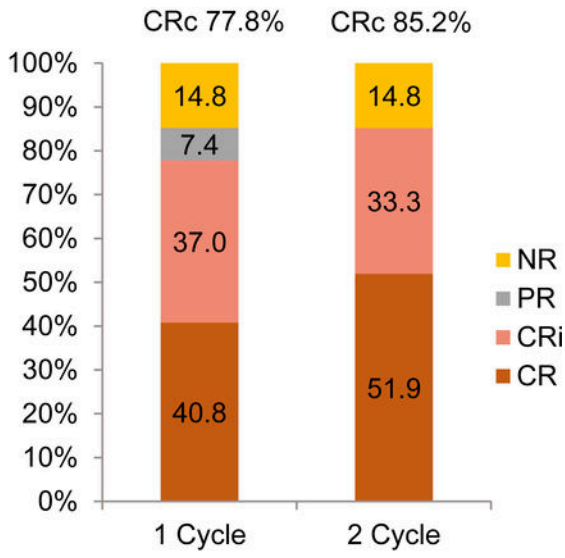

Figure 1

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