Abstract: P1894

Title: AZACITIDINE COMBINED WITH LUSPATERCEPT IN ELDERLY PATIENTS WITH HIGHER-RISK MYELODYSPLASTIC SYNDROME: RESULTS OF AN OPEN-LABEL PROSPECTIVE MULTICENTER TRIAL IN CHINA

Abstract Type: e-Poster Presentation

Topic: Myelodysplastic syndromes - Clinical

Background:

Hypomethylating agents (HMAs) and allogenic stem cell transplant is standard of care for higher-risk MDS (HR-MDS) . However, few elderly(≥60 years) patients are able to pursue an allogeneic stem cell transplant for potential cure of the disease. HMAs is superior to treatment with other established regimens and has shown a survival benefit for elderly patients with HR-MDS. However, leukemic transformation remains a significant challenge, and outcomes with these current therapies are still dismal.Luspatercept has demonstrated efficacy and safety in lower-risk MDS patients. We therefore aimed to evaluate the safety, tolerability, and preliminary activity of azacitidine combined with luspatercept for elderly HR-MDS.

Aims:

Methods:

We did an open-label prospective multicenter clinical trial. Elderly treatment-naive patients (≥60 years) with higher-risk MDS patients (IPSS-R≥3.5) unsuitable for allogeneic hematopoietic stem cell transplantation were enrolled. Azacitidine was administered on days 1–7 of each 28-day cycle at 75 mg/m2/day subcutaneously, and luspatercept was administered subcutaneously on day 8 of each 28-day cycle at 1mg/kg. BM assessments were performed at the end of cycles 1, 2, 4, and 6, then every three cycles thereafter.Responses were assessed per modified 2006 International Working Group (IWG) criteria. The adverse events (AEs) were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.03.

Results:

Between January 2023 and November 2023, 12 patients were enrolled in the trial.Median follow-up was 3（range,1-12）months. The baseline and clinical characteristics of 12 patients are summarized in Table 1. Patients received a median of 3 cycles (range, 1–6) .The overall response rate was 75%(n=9) with 33% (n=4)achieving CR. The median time to first response for mORR was 1 months (range,1–2).5 hematological improvements. Additionally 6(50%)patients achieved post-baseline transfusion independence (TI) for both RBC and platelet. 1 (8%) patients progressed to AML with time to AML progression of 3 months. Adverse events were similar to those reported for azacitidine monotherapy, with the most common grade ≥ 3 adverse events being neutropenia. One patient died from pulmonary infection combined with respiratory failure.

Table1. Baseline patient characteristics

characteristics	**Patients（n=12）**
Age(years)	67 (54-91)
Male	9
Female	3
Absolute neutrophil count (×109/L)	0.88(0.42-2.2)
Hemoglobin(g/L)	68(45-133)
Platelets (×109/L)	74(16-218)
Bone marrow blast (%)	0(0-19)

characteristics	**Patients（n=12）**
WHO 2016 diagnosis	
MDS-EB1	1
MDS-EB2	6
MDS-MLD	5
IPSS-R	
Intermediate	5
High	3
Very high	4
Molecular	
TP53 mutation	4
TET2 mutations	2
DNMT3 mutations	2
Unknown	4

Summary/Conclusion:

Azacitidine combined with luspatercept therapy seems to be a novel, well-tolerated regimen with promising activity in elderly patients with higher-risk myelodysplastic syndrome.

Keywords: Myelodysplastic syndrome, High risk, Azacitidine