Abstract: P1749

Title: EFFICACY AND SAFETY OF MITOXANTRONE HYDROCHLORIDE LIPOSOME COMBINED WITH CLAG REGIMEN IN REFRACTORY AND RELAPSED ACUTE MYELOID LEUKEMIA (NON-M3)

Abstract Type: e-Poster Presentation

Topic: Acute lymphoblastic leukemia - Clinical

Background:

Refractory and relapsed AML carries a poor prognosis with currently no standard salvage treatment. Intensive chemotherapy followed by allogeneic hematopoietic cell transplantation (allo-HSCT) are the most common treatments. CLAG ± M/I regimen [cladribine + cytarabine (Ara-C) + granulocyte colony-stimulating factor (G-CSF) ± mitoxantrone (Mito)/ daunorubicin (IDA)] is one of the commonly used chemotherapy regiments. Mitoxantrone hydrochloride liposome (Lipo-MIT) is the first approved mitoxantrone nano-drug, which has demonstrated favorable pharmacokinetic characteristics and shown preliminary efficacy in AML. From August 2011 to June 2013, a Phase IA clinical study of Lipo-MIT was conducted at the Cancer Hospital Chinese Academy of Medical Sciences, suggesting that the safety of Lipo-MIT was superior to mitoxantrone.

Aims:

To explore the efficacy and safety of Lipo-MIT combined with CLAG regimen in refractory and relapsed AML.

Methods:

We performed a retrospective analysis of pts with refractory and relapsed AML, who received Lipo-MIT combined with CLAG regimen between June 2022 to January 2024. Pts aged 60 years with confirmed diagnosis of refractory and relapsed AML were eligible for inclusion, except acute promyelocytic leukemia (APL). The median dose of Lipo-MIT in the regimen was 18 mg/m2. Efficacy was assessed by composite complete remission (CRc) rate, minimal residual disease (MRD) negative rate, relapse-free survival (RFS) and overall survival (OS). Adverse events were assessed by Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

Results:

16 pts were enrolled with a median age of 44.0 (range 10.0-58.0) years. Eight pts had primary refractory AML and 8 pts had relapsed AML. Risk stratification based on cytogenetic and molecular abnormalities was available for 16 pts: 3 (18.8%) favorable risk, 6 (37.5) intermediate risk, and 7 (43.8) adverse risk. Targeted sequencing was performed on 81.2% of pts (13/16). CEBPA was the most commonly mutated gene found in 25.0% (4/16), followed by NPM1 mutated in 18.8%, IDHI in 12.5%, and IDH2 in 12.5%. The detailed baseline characteristics of patients are shown in Table 1. Twelve pts received 1 cycle of treatment, 4 received 2 cycles. The CRc rate was 68.8% (11/16, 95%CI 36.05%-80.88%). In the pts with CRc, flow cytometric MRD -negative was attained in 9 (81.8%) of pts. Median follow-up was 4.42 (0.89-20.11) months. Of the 11 CRc pts, 7 pts underwent haploid donor HSCT and is still in remission, 3 pts relapsed, and 1 died for an unknown reason. The median RFS was 17.05 months (range, 0.59-17.05 months), and the median OS has not yet been reached (Figure 1). The common grade 3 and above treatment-related adverse events (TRAEs) were hematological toxicities (100.0%), febrile neutropenia (43.8%), sepsis (18.8%) and pulmonary infection (12.5%). TRAEs with an incidence ≥10% are shown in Table 3. The median duration of neutrophil counts 0.5×109 was 24 days (range 14-41) and platelet counts 20×109 was 18 days (range 3-59).

Table1. Baseline characteristics

Characteristic	N=16
Median age (range), years	44 (10-58)
Male,n(%)	9(56.2)
Disease status, n(%)	
Primary refractory	8(50.0)
Relapsed	8(50.0)
FAB classification, n (%)	
AML-M1	4(25.0%)
AML-M2	4(25.0%)
AML-M4	4(25.0%)
AML-M5	3(18.8%)
Others	1(6.2%)
Baseline neutropenia, n(%)	
Grade 3	3(18.8%)
Grade 4	8(50.0%)
Cytogenetic and molecular abnormalities risk category, no(%)	
favorable	3(18.8%)
intermediate	6(37.5%)
adverse	7(43.8%)
Genetic mutations, n(%)	
CEBPA	4(25.0)
NPM1	3(18.8)
IDH1	2(12.5)
IDH2	2(12.5)
FLT3-ITD	1(6.2)
Transfusion dependent at baseline, n(%)	
Red blood cells	4(25.0%)
Platelets	2(12.5%)

Table 2. Efficacy outcomes

	ALL (N=16)
CR	7(43.8%)
CRi	4(25.0%)
NR	5(31.2)
CRc	11/16(68.8%)
95%CI	41.2%-89.0%

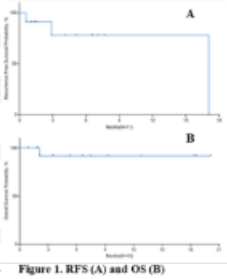

Figure 1. RFS (A) and OS (B)

Table3. Treatment-related adverse events (incidence ≥10%)

Treatment-related adverse events, N(%)	Any	≥G3
Hematologic adverse events		
Neutropenia	16(100.0)	16(100.0)
Anemia	16(100.0)	16(100.0)
Thrombocytopenia	16(100.0)	16(100.0)
Febrile neutropenia	8(50.0)	7(43.8)
Nonhematologic adverse events		
Fever	12(75.0)	1(6.2)
γ-Glutaminyltransferase increased	5(31.2)	0(0.0)
Sepsis	4(25.0)	3(18.8)
Alanine aminotransferase increased	4(25.0)	0(0.0)
Aspartate aminotransferase increased	3(18.8)	0(0.0)
pulmonary infection	3(18.8)	2(12.5)
cough	3(18.8)	0(0.0)
Oral mucositis	3(18.8)	0(0.0)
Novel coronavirus infection	2(12.5)	0(0.0)
Fungal pneumonia	2(12.5)	0(0.0)
Nausea	2(12.5)	0(0.0)
Diarrhea	2(12.5)	0(0.0)
Anaphylaxis	2(12.5)	0(0.0)

Summary/Conclusion:

Lipo-MIT combined with CLAG regimen has a encouraging efficacy and manageable safety profile in refractory and relapsed AML. Therefore, it is necessary to expand the sample size for further validation in the future.

Keywords: Acute myeloid leukemia, Mitoxantrone