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ELEVENTH ANNUAL MEETING

A Multi-institutional Analysis of Outcomes in Acute Myeloid Leukemia Patients with Central Nervous System Involvement

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INTRODUCTION

- Central nervous system (CNS) involvement in acute myeloid leukemia (AML) has been understudied due to the lack of guidelines for screening and treating in this population
- In this study, we evaluated the treatments and outcomes of CNS AML patients at two large academic institutions

AIM

- To evaluate the outcomes of AML patients with CNS involvement at two academic institutions
- To investigate CNS specific outcomes such as efficacy of intrathecal (IT) therapy, number of doses needed for cerebrospinal fluid (CSF) clearance, the extent of neurologic symptom improvement post-treatment, and the impact of IT therapy on overall survival (OS)

METHOD

- Retrospective electronic chart review of adult AML patients from years 2011-2022
- CNS AML was defined as the presence of leukemic blasts in the CSF (identified by either flow cytometry or conventional cytology) or suspicious imaging findings and/or neurologic symptoms with atypical immature myeloid cells in the CSF
- Continuous patient-, disease-, and treatment-related variables were summarized by the median and range, whereas categorical variables were summarized by n (%). The Kaplan Meier method was used for calculation of OS and time to CSF clearance

RESULTS

Baseline Characteristics

- Common risk factors previously associated with CNS involvement were enriched in our population including: monocytic differentiation (40%), elevated lactate dehydrogenase (LDH) levels (67%), and a white blood cell (WBC) count > 40 x 10^9/L (65%).
- The most prevalent AML associated gene mutation was in *FLT3* (46%), followed by *TET2* and *NPM1*, each identified in 27% of patients

Table 1: Baseline characteristics at AML diagnosis

	N = 52
Age at diagnosis, median (range)	60 (23-78)
Gender, N (%)	
Female	27 (52%)
Ethnicity, N (%)	
White	25 (48%)
Black	10 (19%)
Hispanic	6 (12%)
Asian	5 (10%)
ELN risk 2022	
Favorable	7 (13%)
Intermediate	15 (29%)
Adverse	28 (54%)
Type of AML, N (%)	
De novo	44 (85%)
Secondary MDS or MPN	6 (12%)
Acute promyelocytic leukemia	2 (4%)
Monocytic differentiation, N (%)	21 (40%)
LDH > 220 U/L, N (%)	35 (67%)
WBC > 40 x 10^9/L, N (%)	34 (65%)
WBC at diagnosis, x 10^9/L median (range)	72 (0-320)
BM blasts percentage on diagnostic BM, median (range)	78 (6-94)
PB blast at baseline, median (range)	56 (0-98)
Mutations at diagnosis, N (%)	
FLT3	24 (46%)
TET2	14 (27%)
NPM1	14 (27%)
DNMT3A	10 (19%)
ASXL1	9 (17%)
SRSF2	7 (13%)
RUNX1	7 (13%)
KRAS	7 (13%)

CNS Characteristics

- Neurologic symptoms were reported in 69% of patients, with headaches (33%) being the most frequent complaint, followed by vision changes (25%), radicular pain (10%), and altered mental status (10%)

Table 2: CNS AML characteristics

	N = 52
Positive diagnostic finding, N (%)	
CD34+ blasts in CSF	41 (79%)
Atypical myeloid cells in CSF	11 (21%)
Positive imaging findings, N (%)	14 (27%)
CNS disease timing, N (%)	
Before induction	4 (8%)
During induction	25 (48%)
At relapse/refractory	23 (44%)
Neurologic symptoms in preceding 3 months, N (%)	36 (69%)
Headache	17 (33%)
Vision changes	13 (25%)
Radicular pain	5 (10%)
AMS	5 (10%)
Focal neurological deficit	4 (8%)
Hemorrhage	4 (8%)
Vertigo	3 (6%)
Hearing loss/tinnitus	3 (6%)
Seizure	2 (4%)

Treatment

- The median number of total IT doses was 4, ranging from 0-31

Table 3 Therapy received

Therapy	N = 52
Systemic chemotherapy, N (%)	
7+3	28 (54%)
7+3+midostaurin	9 (17%)
HMA+VEN	6 (12%)
HMA single agent	4 (8%)
Intrathecal therapy, N (%)	
Methotrexate	47 (90%)
Cytarabine	37 (71%)
Both	34 (65%)
Number of IT doses received, median (range)	4 (0-31)
Number of IT doses received, N (%)	
0	1 (2%)
1	5 (10%)
2-5	22 (43%)
6-10	11 (21%)
11-15	7 (13%)
15+	5 (10%)

Outcomes

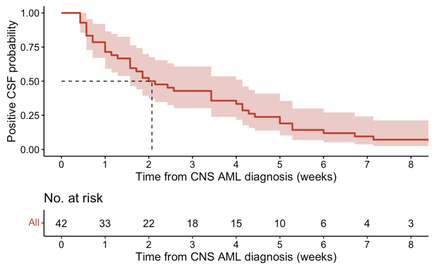
- 84% achieved CSF clearance after a median of 1 IT dose (range: 1-9) and a median time to clearance of 2.07 weeks
- 21% experienced a CSF relapse, with 67% of these patients experiencing concurrent bone marrow relapse
- Patients with CSF relapse received a median of 5 doses of IT therapy before CSF clearance and received a median of 14 total IT doses. In contrast, patients without CSF relapse had a median of 1 IT chemotherapy before CSF clearance and a median of 4 total IT doses
- 69% had documentation supporting improvement in neurologic symptoms following IT therapy
- The median OS was 9.3 months (6.5 - Not reached, 95% CI) for patients diagnosed with CNS involvement before/during induction and 3.5 months (2.0 – Not reached, 95% CI) for patients diagnosed at relapse

Table 4 Outcomes

Outcomes	N = 49
CSF clearance, N(%)	42 (84%)[a]
Number of IT doses before CSF clearance, median (range)	1 (1-9)
CSF relapse, N(%)	9 (21%)[b]
Concurrent BM relapse, N(%)	6 (67%)[c]
Improvement in neurologic symptoms, N(%)	22 (69%)[d]

[a]Out of 49 patients. 2 patients never had repeat LP and 1 was lost to follow-up
[b]Out of the 42 patients that achieved CSF clearance
[c]Out of the 9 patients with CSF relapse
[d]Out of 32 patients with baseline neurologic symptoms who received IT therapy and clear documentation of outcomes post therapy.

Figure 1: Time from CNS AML diagnosis to CSF clearance (weeks)



CONCLUSIONS

- IT therapy was effective in rapidly clearing CSF blasts and improving neurologic symptoms in a majority of patients
- A small subset of patients experienced CSF relapse which typically occurred in conjunction with bone marrow relapse
- Patients with CSF relapse took longer to achieve CSF clearance and received numerically more total IT doses as compared with patients who did not have CSF relapse

CONTACT INFORMATION

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