blood

ACUTE MYELOID LEUKEMIA - THERAPY, EXCLUDING TRANSPLANTATION POSTER I | NOVEMBER 20, 2009

High Prevalence of FLT3 - ITD Mutations in Patients (pts) with Acute Myeloid Leukemia (AML) Who Present with Central Nervous System (CNS) Relapse.

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Abstract

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Despite achievement of complete remission (CR) rates of 70% with modern chemotherapeutic regimens, most pts with AML eventually relapse. CNS extramedullary relapses have become uncommon with the use of high-dose cytarabine (HDAC; > 1.0 g/m^2) containing regimens. The clinical and molecular features associated with a higher risk of CNS relapse are not defined. We analyzed adults who presented with AML and CNS relapses from 2005 until 2009. CNS leukemia was diagnosed by the presence of leukemic blasts in a cytocentrifuge preparation of cerebrospinal fluid (CSF). Patients with blasts in the CSF together with high numbers of red blood cells (> 5) were not considered to have CNS disease if the blasts were high in the peripheral blood (5 × 10^9/L). All pts with evidence of CNS disease underwent a marrow examination. There were 10 pts with a diagnosis of AML and CNS relapse observed during the above mentioned time period. Median age was 38 years (range 23-56) and 80% were female. At time of first diagnosis the median WBC was 61×10^9/L and 50% had M4/M5 phenotype by FAB. Six pts

had received induction chemotherapy containing standard doses of cytarabine; five of them received HDAC as consolidation courses afterwards. Four pts received induction regimens containing HDAC. The CR rate was 80% (8 of 10 pts). The median CR duration was 6 months (range 3-7). CNS involvement was detected at a median of 8 months after diagnosis (range 5-29). No pt had isolated CNS relapse. CNS disease was detected in the setting of refractory AML (N=2), 1st systemic relapse (N=4) or 2nd and subsequent relapses (N=4). Eight pts had neurologic symptoms at time of CNS relapse, including headache (N=3), involvement of cranial nerves (N=2), visual impairment (N=1), seizures (N=1), confusion (N=1) and feet neuropathy (N=1) (one pt had more than one symptom). CNS imaging was done in 8 pts, and three pts had abnormal findings by MRI suggestive of CNS disease. The median cell count on CSF was 305 (range 0-880) and median blast percentage was 89%. Two pts had zero cells with blasts detected on cytocentrifuge preparation only. None of the 2 pts had circulating blasts and both had abnormal findings on brain MRI suggestive of CNS relapse. Cytogenetic information was available at initial diagnosis for 9 pts, being diploid in 6 pts. The pt without cytogenetic information was diploid at time of relapse. FLT3 mutation status was unknown at time of diagnosis in six pts, being positive for the ITD mutation in 4 pts. At time of 1st relapse, FLT3 mutation status was positive in 8 pts (80%; all cases were FLT3-ITD). Treatment for CNS disease consisted of intrathecal chemotherapy (methotrexate alternating with cytarabine) in all pts and whole brain radiation therapy in one (24 Gy in 12 fractions). Therapy was successful in clearing all signs of CNS disease in 9 pts. One pt persisted with disease after 4 intrathecal injections and expired 6 weeks afterwards. Five pts had additional CNS relapses at a median of 3 months (range 2-15) after being first diagnosed with CNS disease. Stem cell transplantation (SCT) was done in 3 pts, 2 with active disease and one in CR. All three relapsed with CNS disease after SCT. Only one pat currently remains alive and with active disease. Median survival after CNS relapse was 3 months (range 1-28). In conclusion, CNS relapse is a rare occurrence in AML and is associated with a poor prognosis. A high prevalence of FLT3-ITD mutations was observed in these pts; FLT3 mutations are associated with elevated WBC counts, which are traditionally considered a risk factor for CNS relapse. Analysis of merged data from larger databases may help to better discern the association between FLT3-ITD mutations and CNS relapse. If confirmed, prophylactic measures might be considered for such pts.

Disclosures:

Jabbour: *Novartis:* Speakers Bureau; *Bristol Myers Squibb :* Speakers Bureau.

Author notes

* Asterisk with author names denotes non-ASH members.