

Table 1 Clinical characteristics of patients who had a CNS relapse

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13
Age, years	47	63	54	40	57	55	47	47	60	65	51	20	33
Gender	M	M	M	M	M	F	F	M	F	F	M	M	M
WBC count, $\times 10^9/L$	27	1.5	25	33	33	3	0.6	31	1.9	0.4	15	2.2	1.9
HGB, g/L	122	120	84	130	133	119	51	101	86	51	109	81	130
PLT count, $\times 10^9/L$	20	60	13	16	22	60	9	29	56	34	16	4	70
Fibrinogen, mg/dL	84	237	124	116	50	52	60	51	70	280	74	69	141
D-dimer, ug/mL	17.90	4.03	14.43	39.05	2.98	14.33	59.83	3.32	5.19	4.92	24.41	59.83	4.81
FLT3-ITD mutation	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	No	Yes
Prior known CNS involvement	No	No	No	No	No	No	No	No	No	No	No	No	No
Intracranial bleeding	No	No	No	During induction	No	Before induction	No	No	No	During induction	During induction	During induction	During induction
Induction treatment	ATRA+ RIF	ATRA+ RIF	ATRA+ RIF	ATRA+ ATO	ATRA+ ATO	ATRA+ ATO	ATRA+ RIF	ATRA+ ATO	ATRA+ ATO	ATRA+ ATO	ATRA+ ATO	ATRA+ ATO	ATRA+ ATO
Chemotherapy in post-remission treatment	No	No	No	No	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes
Intrathecal therapy	Yes	No	Yes	Yes	Yes	No	No	Yes	No	No	Yes	No	No
Time to CNS relapse, months	10	24	11	24	12	15	32	7	29	11	37	39	22
BM relapse	No	No	No	Yes	No	No	Yes	No	No	Yes	No	No	Yes
Outcome at last follow-up	CR	CR	Death	CR	Death	Death	CR	CR	Death	Death	PR	CR	Death
Overall survival, months	20+	26+	11	36+	33	26	137+	150+	29	33	38+	135+	23

CNS, Central nervous system; WBC, white blood cell; HGB, hemoglobin; PLT, platelet; FLT3-ITD, Internal tandem duplication of FMS-like tyrosine kinase-3; BM, bone marrow; ATRA, all-trans retinoic acid; ATO, arsenic trioxide; RIF, Realgar-Indigo naturalis formula; IDA, idarubicin; CR, complete remission; PR, partial remission.

Table 2 Characteristics of CNS relapsed patients during different periods

Characteristics	2011-2015 (n=284) N (%) /median [range]	2016-2023 (n=626) N (%) /median [range]	P Value
CNS relapse (n=13)	6 (2.1)	7 (1.1)	0.384
Age, years	47 [20-65]	54 [40-63]	0.331
Gender			0.266
M	3 (50.0)	6 (85.7)	
F	3 (50.0)	1 (14.3)	
WBC count, $\times 10^9/L$	1.9 [0.4-31]	25 [1.5-33]	0.063
HGB, g/L	83.5 [51-130]	120 [84-133]	0.028
PLT count, $\times 10^9/L$	31.5 [4-70]	20 [13-60]	0.886
Fibrinogen, mg/dL	70 [50-280]	80 [50-240]	0.886
D-dimer, ug/mL	5.1 [3.3-59.8]	14.4 [3.0-39.0]	1.000
FLT3-ITD mutation	2 (33.3)	6 (85.7)	0.103
Intracranial bleeding	3 (50.0)	3 (42.9)	1.000
Death	3 (50.0)	3 (42.9)	1.000

CNS, Central nervous system; WBC, white blood cell; HGB, hemoglobin; PLT, platelet; FLT3-ITD, Internal tandem duplication of FMS-like tyrosine kinase-3.

Table 3 Multivariate analysis on CNS relapse

Variable	OR (95% CI)	P Value
FLT3-ITD mutation	5.069 (1.105-23.247)	0.037
Intracranial bleeding	17.747 (2.725-115.572)	0.003
Fibrinogen	0.363 (0.111-1.187)	0.094

CNS, Central nervous system; FLT3-ITD, Internal tandem duplication of FMS-like tyrosine kinase-3.
Bold values are statistically significant.

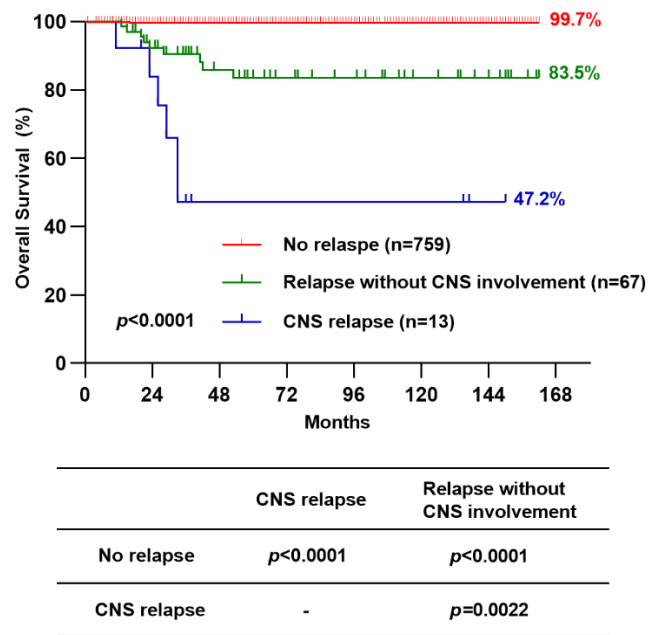


Figure 1 Overall survival of non-relapsed APL patients and relapsed patients with or without CNS involvement