

Results of treatment of relapsed promyelocytic leukemia in children using chemotherapy and arsenic trioxide (ATO) followed by autologous SCT (ASCT)

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On behalf of the Russian-Byelorussian Pediatric APL study group

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Abstract

The Russian multicenter APL-2003 protocol for pediatric APL demonstrated a non-inferior outcome compared with the APL-93/98 studies despite a reduction of ATRA to 25 mg/m² and cumulative anthracycline dose to 405 mg/m²: at a median follow up of 35 mo the EFS and OS were 0.79±0.6 and 0.93±0.3. Seven relapses (11.9%) occurred out of 61 patients (pts) at a median of 21 (4–35) mo. Second remission was induced with diverse therapy (Table 1) and consolidated with 14 ATO at 0.15 mg/kg per day; in 1 pt gemtuzumab ozogamicin (GO) at 6 mg/m² was added to ATO. All pts achieved 2nd hematological remission and PML/RAR α negativity in bone marrow either after induction (3 pts) or after consolidation (4 pts). HDARaC + G-CSF were used for additional "in-vivo purging" and PBSC mobilization. Harvesting was successful in all pts: a median of CD34+ dose 17 (8–40) x 10⁶/kg was achieved after single apheresis. In all cases, apheresis product proved to be PML/RAR α negative. AHSCT was performed in 6 pts after conditioning with HDARaC + Mel180 mg/m² in 4 pts, Bu12mg/kg + Mel 140 mg/m² in 1 pt and Treosulfan 42 mg/m² + Mel140 mg/m² in 1 pt. All pts engrafted at a median of 16 (12–25) d with minimal transplant-related toxicity. Three pts received GO on day +100 after ASCT with minimal toxicity. Two pts with skin involvement received complementary electron beam skin irradiation. At a median of 26 mo 6 pts continued in molecular remission and 1 pt experienced 2nd relapse. We conclude that children with relapsed APL can be treated effectively with chemotherapy, ATO, and ASCT.

Table 1

Case №	1	2	3	4	5	6	7
Age in years	14	13	1	14	7	12	13
WBC at Dx mm ³	1.400	3.900	57.000	15.700	2.600	40.000	0.900
Rx start – relapse, mo	21	29	9	35	23	4	12
PML/RAR α before maintenance	+	+	-	+	-	+	-
Relapse site	bone marrow	bone marrow	bone marrow	bone marrow skin	bone marrow	bone marrow skin	bone marrow
2 nd remission induction	ATRA ATO	ATRA 7+3	ATRA HDARaC Mitox	ATRA AraC, Ida	ATRA ATO Mitox	ATO	ATO
Post 2 nd remission therapy	ATO 2 courses	ATO 3 courses	ATO 3 courses	ATO 3 courses	ATO 3 courses	ATO GO	ATO 1 course
Auto-HSCT	+	+	+	+	+	+	
Duration of 2 nd mol remission mo	+ 35	+ 27	+ 26	+ 26	+ 18	+ 18	+ 1

Keywords: promyelocytic leukemia, arsenic trioxide, autologous hematopoietic stem cell transplantation