SORAFENIB WITH ATRA PLUS CHEMOTHERAPY IN HIGH RISK FLT 3 POSITIVE APL

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Introduction:
Acute promyelocytic leukemia (APL) is a unique subtype of acute leukemia characterized by abnormal proliferation of promyelocytes, life-threatening coagulopathy, and the chromosome translocation t(15;17)(q22;q11-12), which results in the PML-RARα fusion protein. This protein destabilizes homeostasis, maturation and hampering the maintenance and differentiation of hematopoietic cells into different lineages, fixing cells in the promyelocyte stage. *FLT3* is a gene that belongs to the class III receptor tyrosine kinase (RTK) family. RTKs are well correlated with cell proliferation, and *FLT3* mutations are recurrently associated with AML prognosis. As a result, the tyrosine kinase domain is permanently activated, regardless of ligand, which leads to the uncontrolled proliferation of myeloid cells. This deregulated activation impairs hematopoiesis and will contribute to leukemogenesis. *FLT3* mutations are present in approximately 2% to 38% of APL cases, depending on ITDs or mutations in the tyrosine kinase domain. *FLT3* mutations have been identified as being highly related to hyper leucocytosis. Material and methods: we described two male patients with high-risk APL pml/rar alpha and Flt-3 positive. Patient 1: F.N. 16 years old male presented with hyper leucocytosis WBC:191,Hb 89 Plt:21 and severe hemostasis disorder with hypofibrinogenemia and hemorrhagic syndrome. Patient 2: M.D. 40 year old male, with hyperleukocytosis WBC 53,2 Hb 86 Plt 33. As a high-risk APL we introduce induction therapy with ATRA 45mg/m2 and chemotherapy consisted ARA-C 100mg./m2 (7 days) and antracyclin (Idarubycin). From day +1 we add Sorafenib multi-kinase inhibitor in dose 400mg. during a 14 days. Results: after induction therapy both patient are in complete hematologic and molecular remission. PML-RARA and FLT-3 negative. After consolidation therapy they are still in CR. Conclusion: Addition of Sorafenib to standard ATRA plus chemotherapy regimen in high-risk Flt-3 positive APL leads to complete remission and good outcome in this fatal form of acute leukemia.