only 7/24 (29%) pts with FLT3 mutations (one patient with M0 and normal karyotype, one with M5a and also normal karyotype, 3 pts with M3 and translocation (15; 17), one patient with M2 and deletion 19, one with M4 and inv16). FLT3/ITD+ pts had significantly higher WBC count at diagnosis (WBC count for FLT3/ITD+ was 73.5×10^9/L and WBC count for FLT3/ITD- was 14.9×10^9/L, $p<0.05$). Median of overall survival of the whole group of pts was 11 months, and median of survival of pts with FLT3 mutations was 6 months. *Conclusion*: In contrast to other reports incidence of FLT3/ITD and D835 mutations are lower in our cohort although the study group was small and performed in a single Institution. With a median follow up of 46 months remission duration and overall survival were significantly shorter for patients with FLT3 mutations.

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MONITORING OF CARDIOTOXICITY DURING INDUCTION CHEMOTHERAPY CONTAINING IDARUBICIN IN ACUTE MYELOID LEUKEMIA WITH CIRCULATING MARKERS

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Backgrounds. Cardiac toxicity is a well-known and serious complication of antitumorous treatment. Anthracyclines represent the greatest risk for development of cardiotoxicity. Recently, circulating markers of structural and functional myocardial damage have been gaining ground in cardiotoxicity diagnostics. *Aims.* Monitoring of cardiotoxicity during induction chemotherapy in acute myeloid leukemia (AML) patients and assessment of the potential for use of circulating markers in early diagnostics of cardiotoxicity. *Methods.* Fifteen consecutive adult patients with a newly diagnosed AML (9 male and 6 female, mean age 43.7±10.6 years) participated in the study. The patients received induction chemotherapy containing intermediate doses of cytarabine and idarubicin (IDA) 12 mg/m^2/day intravenously on day 1, 3 and 5 (in total 36 mg/m^2 = 1/4 of the maximum recommended cumulative dose). From circulating markers of myocardial damage we used a marker of cardiac dysfunction and failure - N-terminal pro brain natriuretic peptide (NT-proBNP), and two markers of myocardial necrosis (cardiospecific markers) - cardiac troponin T (cTnT) and creatine kinase MB (CK-MB mass). Serial measurements of plasma NT-proBNP concentrations were performed at the baseline, the day following each IDA infusion, after 14 days and after circa 1 month, i.e. before the next chemotherapy. Cardiospecific markers (cTnT, CK-MB mass) were measured at the baseline and after the last IDA infusion. *Results.* The mean baseline concentration of NT-proBNP in newly diagnosed AML patients was 129.7±59.6 pg/mL. The mean NT-proBNP concentration increased after the first IDA infusion to 307.3±171.4 pg/ml (p=0.02). In most of the patients, the second and the third IDA infusions were not associated with a further increase in the NT-proBNP value and values after 2 or 4 weeks were not significantly different from the baseline. However, in one of the patients the NT-proBNP values were increasing after each IDA infusion (after the last one 786.2 pg/ml) and within 14 days he developed congestive heart failure due to left ventricular diastolic dysfunction as assessed by echocardiography. At that time, the NT-proBNP value was 1184.0 pg/ml; after diuretics it decreased significantly. In all patients, plasma cTnT and CK-MB mass concentrations were within the reference interval at the baseline and after the induction chemotherapy. *Conclusions.* Our results show that induction chemotherapy in AML (IDA 36 mg/m^2 and intermediate doses of cytarabine): 1. does not cause detectable damage of cardiomyocyte structure, 2. is in all patients associated with acute neurohumoral activation (transient elevation of NT-proBNP) indicating acute subclinical cardiotoxicity, 3. may lead to congestive heart failure and NT-proBNP seems to be a promising early marker and predictor of this complication.

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WT-1, BCL2 AND BAX EXPRESSION AND CLINICAL OUTCOME IN PATIENTS WITH ACUTE MYELOID LEUKEMIA

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Background and aims. We prospectively evaluated the impact of WT-1, BCL2 and BAX expression on the clinical history of patients with non M3 AML and present here our preliminary results. *Patients and methods*. Forty patients have been included in the study. Complete molecular data are at the present available of 15 patients. Median age was 55 years (range 24-73); the cytogenetic evaluation at diagnosis (14 patients) disclosed a normal karyotype in 9 patients, a complex karyotype in 3 and other abnormalities in 2. All patients received as induction therapy fludarabine, Ara-C, idarubicin plus etoposide; 13 achieved CR (3 after second line therapy), 2 were refractory. All patients in CR received consolidation chemotherapy (13) or were submitted to autologous or allogeneic stem cell transplant. CR lasted a median of 14.5 months (range 3-48). Five patients have relapsed after a median of 8 months (range 3-17). At this moment 10 patients are alive and disease free in first or second CR. Median survival for the whole series of patients is 18 months (range 8-50. By real time PCR we studied the expression of WT-1, BCL2 and BAX on marrow samples collected at diagnosis, at evaluation of response to induction and every 6 months, in the follow up and tried to correlate molecular data with clinical outcome. *Results*. We classified patients in 3 groups according to the expression at diagnosis of WT-1 and BCL2. The 3 patients with absent or low expression of WT-1 and BCL2 at diagnosis maintain CR at 28, 30 and 48 months. Four out of the 5 patients with high expression of WT-1 or BCL2 at diagnosis achieved CR; 1 did not respond to induction therapy. Among the responsive patients 1 has died in CR after 17 months for transplant related complications, 2 have relapsed (at 11 and 14 months from diagnosis) and 1 mantains CR. Of the 3 patients with high expression of both WT-1 and BCL2 at diagnosis 1 did not respond to therapy, 2 achieved CR (in one patient lasted 7 months, in the second still ongoing at 12 months). Whereas the expression of BAX at diagnosis doesn't seem to correlate with outcome, the level of BCL2 expression may have a relevant prognostic value. The 3 patients mantaining the first CR at 28-48 months had low levels af BCL2 expression at diagnosis. On the contrary patients with high levels of BCL2 had a poor outcome: one did not respond to therapy, other two showed a chemorefractory relapse at 7 and 15 months from diagnosis. The longitudinal evaluation of BAX-BCL2 ratio may give information on the relapse risk, with the progressive reduction of this ratio indicating impending relapse. The increase in BCL2 and therefore the reduction of BAX-BCL2 ratio may precede of some months the increase of WT1. *Conclusion*. These preliminary results indicate that molecular evaluation at diagnosis of WT-1, BCL2 and BAX might have prognostic value and that prospective comparative evaluation of BAX-BCL2 ratio might predict relapse.

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PROGNOSTIC RELEVANCE OF SOLUBLE TPO LEVEL IN AML

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Backgrounds. Thrombopoietin (TPO), the major growth factor for cells of the megakaryocytic lineage is removed from circulation by binding to c-mpl receptors present on platelets and megakaryocytes. Recently functioning c-mpl receptors was reported on the AML blast cells and its clinical impact on AML prognosis remains to be characterized. *Aim.* Is to determine the level of TPO in AML patients in order to characterize its clinical relevance. *Methods.* We assessed TPO levels by ELISA in 41 AML patients at diagnosis, after 28 days of induction chemotherapy and at AML remission. Follow up for the patients was done up to 24 months. *Results.* TPO levels was significantly higher at diagnosis as compared to normal controls ($p<0.01$). At 28 days after induction chemotherapy the TPO level continue to elevate and was significantly higher as compared to the diagnosis level ($p<0.01$) ,and then decline during remission reaching near the control level ($p>0.05$). The TPO levels was inversely correlated to the platelets counts (R=0.9 , $p<0.01$). TPO level at AML diagnosis was significantly lower in a group of patients who died during the follow up course(n= 25) and in patients resist induction chemotherapy (n=8) as compared to patients who survive and patients who respond to chemotherapy ($p<0.05$ for both).

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IMPACT OF ADDITIONAL CYTOGENETIC ABNORMALITIES ON REMISSION INDUCTION RATE,EVENT FREE AND OVERALL SURVIVAL IN 34 PATIENTS WITH NEWLY DIAGNOSED ACUTE PROMYELOCYTIC LEUKEMIA TREATED WITH APL93.TUNISIAN EXPERIENCE

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Additional chromosomal abnormalities in acute promyelocytic