receiving 105 cycles of chemotherapy between June 2012 and December 2016 in Marmara University Pendik Research and Training Hospital. Median patient age was 50 years (18-73); and there was no significant gender difference (38 female *vs* 44 male (46% *vs* 54%)). All patients had active disease, 78 (74.3%) of them received 3+7 (idarubicine - ara-c), 25 (23.8%) of them FLAG-Ida, 1 patient received EMA and 1 patient received CLARA chemotherapy protocol. Acute promyelocytic leukemia was excluded from the analysis. All patients received posaconazole as oral suspension at the dose of 200 miligrams three times daily starting on the first day of chemotherapy. Prophylaxis was continued until marrow regeneration, or occurrence of IFI, or onset of adverse events, or discontinuation due to other reasons. All fungal infections were classified as possible, probable, or proven according to European Organization for the Research and Treatment of Cancer (EORTC) and the Mycoses Study Group (MSG) consensus criteria.

Results: Mean posaconazole prophylaxis duration was 20±13 (1-68) days. This duration was 29.7 days (16-50) in patients receiving prophylaxis until marrow recovery, 18.9 (9-34) days in patients developing IFI under prophylaxis, and 12.7 days (1-68) in prophylaxis discontinuations due to adverse events and other reasons. Posaconazole prophylaxis was administered until marrow recovery without IFI (clinical success rate) in 42 of 105 (40%) chemotherapy cycles. In 18 cycles prophylaxis was stopped after diagnosis of IFI (%17.1). Discontinuations were due to adverse events in 6 cycles (5.7%), and due to other reasons (diarrhea, intolerance of oral medication, recurrent high grade fever, death) in 39 cycles (37.1%). IFI incidence under effective posaconazole prophylaxis was 28.1% (18/64). Total clinical failure rate was 60% (63/105). IFI was diagnosed with pulmonary nodules in 12 of 18 patients (66.6%; EORTC-MSG: possible), with galactomannan positivity in 3 patients (16.6%; EORTC-MSG: probable), and with fungal culture in 3 patients (16.6%; EORTC-MSG: proven). Data from 70 patients were available for mortality analysis. In patients receiving effective posaconazole prophylaxis, all-cause mortality rate at day 100 was (9/44; 20.4%) significantly lower than patients unable to continue posaconazole prophylaxis (12/26; 46.1%) (p:0.023). In the subset of patients receiving prophylaxis as planned; there was no statistically significant difference in IFI incidence between previously untreated AML (13/46; 28.2%) and relapsed/refractory AML (5/18; 27.7%).

Summary/Conclusions: In our real-life experience, we have demonstrated early survival benefit in patients receiving effective posaconazole prophylaxis. Although our IFI rate was comparable to other real-life data, our clinical failure rate was slightly higher. This is probably due to compliance issues, since in many chemotherapy cycles (37.1%) posaconazole was discontinued due to "other reasons" such as drug intolerance. Although not as effective as in the clinical trials; our data still supports the use of posaconazole prophylaxis in high risk AML patients.

PB1682

CLINICAL AND PROGNOSTIC VALUE OF FLT3 MUTATIONS IN ACUTE MYELOID LEUKEMIA PATIENTS IN ROUTINE CLINICAL PRACTICE – SINGLE CENTER EXPERIENCE

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Background: Detection of FLT3 gene mutations in acute myeloid leukemia (AML) now recognized as an unfavorable factor that affects the disease course, emerging the risk of relapses and overall survival (OS) shortening. Although about 30% of AML patients harbor one of the FLT3 gene lesion, at present there are no internationally standardized assays to quantify FLT3 mutation burden and no results of randomized clinical trials intended to individualize AML treatment based on FLT3 status. Some hematologists advocate to allo-SCT as consolidation in FLT3 ITD+ patients, but this way could be hard in frail and old patients and in countries with low access to transplant techniques. On the other hand, the development of target drug therapy – FLT3-kinase inhibitors gives us a new hope for improvement in the treatment results of such poor-prognosis subset of AML patients.

Aims: To assess the frequency of FLT3 gene mutations and its impact on clinical parameters and overall survival of the patients with acute myeloid leukemia (AML) in routine clinical practice.

Methods: We have analyzed FLT3 gene mutation frequencies, complete blood count (CBC) parameters, karyotype and survival outcomes per FLT3-mutation status in 199 patients with AML (83 male / 116 female). The median age at diagnosis was 52 years (20-86 years). To determine FLT3 gene mutations we used the method of polymerase chain reaction (PCR) with subsequent restriction. FLT3 gene mutations were classified as internal tandem duplication (FLT3-ITD) and point mutation in the "A-loop" (FLT3-TKD). Statistical analysis was included Kruskall-Wallis ANOVA and Kaplan-Meyer curves.

Results: We observed next FLT3 gene mutations rates: FLT3-ITD - 22.6% (45/199), FLT3-TKD 5.5% (11/199), FLT3-ITD and FLT3-TKD in combination 1.0% (2/199), other 70.8% (141/199) patients had no mutations (FLT3-). CBC data at the time of diagnosis were as follows (median (max-min)): · FLT3-ITD: Hb 9.7 (3.7-13.0) g/dl, WBC 40.3 (0.6-400.0) x 10^9/l, blasts 80% (21-100), platelets 60 (2-140) x 10^9/L; · FLT3-TKD: Hb 10.2 (5.8-12.8) g/dl, WBC 62.4 (1.7-362.0) x 10^9/l, blasts 68% (23-100), platelets 55 (12-115) x 10^9/L; · FLT3-ITD+TKD: Hb 5.8, 8.4 g/dl, WBC 37.0, 157.0 x 10^9/l, blasts 65%, 86%, platelets 38, 186 x 10^9/L; · FLT3-: Hb 9.0 (2.8-14.0) g/dl, WBC 12.9 (1.0-260.0) x 10^9/l, blasts 64% (20-103), platelets 63 (1-334) x 10^9/L; Significant differences across the groups were seen only in WBC and blasts. Chromosomal aberrations were revealed in 38% of FLT3-ITD, 64% of FLT3-TKD, none of FLT3-ITD+TKD and 51% of FLT3- patients. All patients received chemotherapy (7+3, 5+2, HAM). Transplantation of hematopoietic stem cells (SCT) was performed in 28 (allo/auto 17/11) (14%) patients: FLT3-ITD allo-3; FLT3-TKD allo-1, auto-1; FLT3- allo-13, auto-10. We found significant (p=0.00024) differences regarding to OS between FLT3-ITD, FLT3-TKD and FLT3- patients (Figure 1). Median survival times were: 5.1 months for FLT3-ITD, 7.1 months for FLT3-TKD and 13.0 months for FLT3- patients.

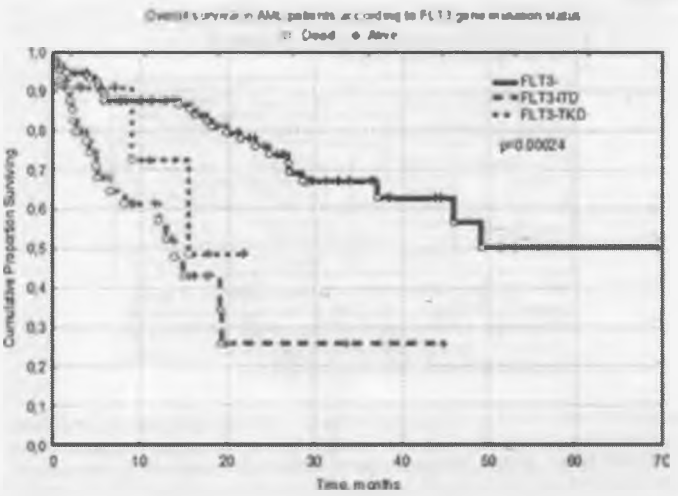

Figure 1.

Summary/Conclusions: We confirmed the role of FLT3 gene mutations as an unfavorable factor for AML patients in routine clinical practice by own experience. The investigation of qualitative assessment potential and target therapy value especially in SCT ineligible FLT3 gene mutations positive patients has of great value for AML management.

PB1683

TARGETING ENDOTHELIAL DYSFUNCTION FOR PROTECTION FROM ANTHRACYCLINE-INDUCED CARDIOTOXICITY IN PATIENTS WITH ACUTE LEUKEMIA AND CO-MORBID ISCHEMIC HEART DISEASE

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Background: Cardiotoxicity of chemotherapeutic drugs, in particular anthracycline antibiotics (AA), is one of the biggest problems in treatment of patients with acute leukemia (AL). Chemotherapy with AA is accompanied by systemic endothelial dysfunction, increasing the cardiovascular toxicity risk and promoting vascular complications. Patients with co-morbid ischemic heart disease (IHD) are at extremely high risk of myocardial injury and in need of anthracycline cardiotoxicity (AC) prevention.

Aims: To assess the effectiveness of L-arginine in the prevention of endothelial dysfunction as a predictor of acute AC in patients with AL and co-morbid ischemic heart disease.

Methods: A total of 66 patients with newly diagnosed acute leukemia (acute lymphoid leukemia – 7 patients, acute myeloid leukemia – 59 patients) and co-morbid ischemic heart disease were included in the study. The cohort consisted of 34 (51.5%) males and 32 (48.5%) females, age of 54–72 years, ECOG I-II. The duration of IHD ranged from 3 to 15 years. Chemotherapy (CT) schemes included AA (doxorubicin). The evaluation of endothelial dysfunction was performed by determining the stable metabolites of nitric oxide – nitrite anions $[NO_2]^-$ and activity of total NO-synthase in serum of patients before the CT and upon reaching a cumulative dose of AA from 100 to 200 mg/m^2 by doxorubicin. The mean total cumulative dose of AA reached 162,04±24,65 mg/m^{2}and 166,49±27,34 mg/m^{2}in groups I and II respectively. The study was approved by the local ethical committee and all patients gave a written consent before they were included in the study. Patients were divided into two groups: (n=36) – AL patients treated with CT; II (n=30) – AL patients, whom during the CT in order for prevention of acute AC were given L-arginine hydrochloride 4.2% 100 ml IV the day before and during administration of AA, followed by oral L-arginine aspartate for a month.

Results: In the debut of AL prior to the CT in all 66 (100%) patients the increased activity of total NOS in 3.8 times compared with the norm ($p<0,001$) was noted, with simultaneously reduced concentration of $[NO_2]^-$ in 1.5 times relatively normal values ($p<0,05$) (Table 1). As a result of two CT courses of remission induction in patients of group I the tendency to reduce the total NOS activity compared with its level before treatment was observed. At the same time the significant decrease of $[NO_2]^-$ in 1.8 times relatively normal values ($p <0.01$) and a trend to lower their content in 1.2 times compared with the data before treatment ($p>0.05$) was noted. These changes constitute the violation of NO-dependent vasodilation mechanism and endothelial dysfunction intensification. Provided achieving low cumulative dose of AA in patients of group II on the background of AC prevention with L-arginine showed a significant decrease in 1.9 times the total NOS activity ($p <0.001$) with a simultaneous tendency to increase concentration of $[NO_2]^-$ in 1.3 times ($p>0.05$) compared to that before treatment.

Table 1.

Indicators of total NOS and $[NO_2]^-$ in AL patients with co-morbid IHD in the CT dynamics

Research groups		$[NO_2]^-$, μmol/L	NOS, μmol/L×min
Practically healthy (n=18)		3,2±0,38	0,61±0,08
pts of group I (n=36)	before CT	2,18±0,31*	2,3±0,14*
	after CT	1,8±0,21*	1,97±0,13*
pts of group II (n=30)	before CT	2,14±0,29*	2,1±0,14*
	after CT	2,4±0,33	1,2±0,11*√δ

Note: significant differences * - between indicators of healthy persons and in the groups ($p<0.05$); √ - between indicators before CT and upon reaching cumulative dose of AA 100-200 mg/m² ($p<0.05$), δ - between indicators of groups I and II in reaching cumulative dose of AA 100-200 mg/m² ($p<0.05$)

Summary/Conclusions: Thus, during the CT with the inclusion of AA without L-arginine in patients with AL and co-morbid IHD we observed the depletion of NO substrate production, accompanied by endothelial dysfunction impairment. The additional appointment of L-arginine on the background of CT can restore synthesis of NO and, respectively, the mechanism of NO-dependent vasodilation, thus reducing the risk of early anthracycline cardiotoxicity development.

PB1684

CLINICAL CHARACTERISTICS AND SURVIVAL OUTCOMES IN ACUTE ERYTHROID LEUKEMIA (AML-M6): AML/MDS WORKING PARTY STUDY OF KOREAN SOCIETY OF HEMATOLOGY

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Background: Acute erythroid leukemia is a morphologically distinct and rare entity designated as M6 in FAB classification. In Korea, patients with AML-M6 have been treated as acute myeloid leukemia with intensive chemotherapy whenever possible rather than as myelodysplastic syndrome. The 2016 revision of the WHO reclassified erythroid/myeloid subtype (a case with ≥50% BM erythroid precursors and ≥20% myeloblasts among non-erythroid cells) to MDS category based on the close biological and genetic relationships between them.
Aims: The aims of this multi-center study were to characterize clinical characteristics and treatment outcomes in patients with newly diagnosed acute erythroid leukemia.
Methods: Clinical data from newly diagnosed M6-AML patients between 2002 and 2012 at 11 academic centers were retrieved from the electronic registry data of AML/MDS working party of Korean Society of Hematology. Conventional cytogenetic analysis was performed on metaphase cells prepared from bone marrow aspirate by G-banding technique. Patients were classified according to the UK MRC cytogenetic risk criteria and the International Prognostic Scoring System (IPSS) risk groups for MDS based on karyotypes. Survival curves were analyzed using the Kaplan-Meier method and compared with a log-rank test. A p-value <0.05 was considered statistically significant.
Results: A total of 84 patients with AEL (M6-AML) as defined by 2008 WHO classification criteria were included in this study. The median age at diagnosis was 55 years with following distribution: age ≤ 49, 34 patients (40.5%); age 50 – 59, 17 (20.2%) patients; 60 – 69, 19 (22.6%) patients; age ≥70, 14 (16.7%) patients. There were 50 (59.5%) males and 34 (40.5%) females. Median hemoglobin, white blood cell count, and platelet count were 8 g/dL, 3.69×10^9/L, and 58×10^9/L, respectively. Peripheral blood blasts were observed in 55 (65.5%) patients. Cytogenetic results were available in 80 patients. Among them, karyotype was normal in 43 (53.8%) and complex in 13 (15.5%) patients, respectively. Trisomy 8 was observed in ten (12.5%) patients. Monosomies of chromosome 5 and 7 were observed in five (6.2%) and four (5.0%) patients, respectively. Four (5.0%) patients had t(9;22)(q34;q11.2). Cytogenetic risk groups according to UKMRC criteria were intermediate in 63 (78.8%) patients, and poor in 17 (21.2%) patients. Seventy-two (85.7%) patients received induction chemotherapy and 55 patients (76.4%) achieved complete remission. Nineteen patients received two or three cycles of induction chemotherapy. Thirty-eight patients (45.2%) underwent allogeneic hematopoietic stem cell transplantation (HSCT): 8 patients, matched-sibling donor; 15 patients, matched-unrelated donor; 5 patients, alternative donor were used. Treatment-related mortality of HSCT was observed in five (17.9%) patients. Fourteen (16.7%) among the study patients relapsed. The median overall survival (OS) of total 84 study patients was 21 months. Patients with intermediate risk karyotype showed better median OS than those with poor risk karyotype (22 months *vs* 7 months, P=0.020). The median OS was similar in patients with good and intermediate IPSS, but significantly worse in patients with poor IPSS (21 months, 27 months, 7 months, respectively, P=0.026) (Figure 1).

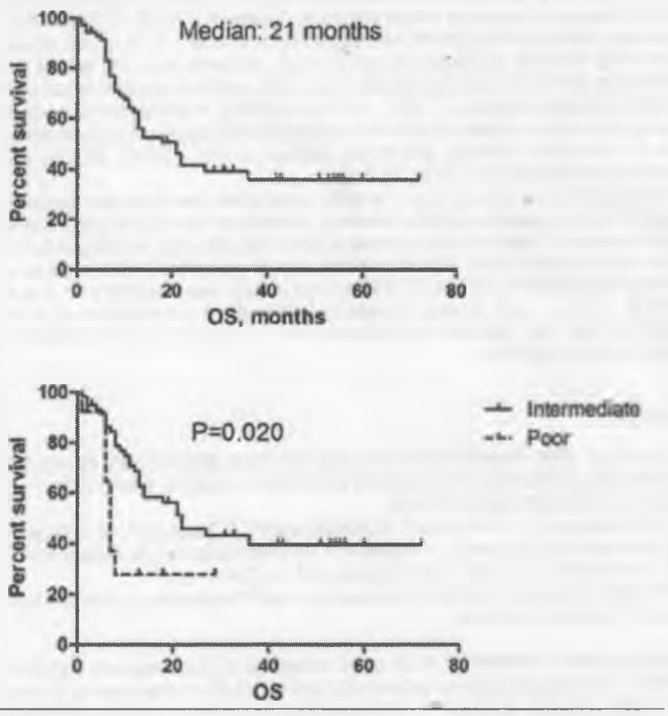

Figure 1.

Summary/Conclusions: Patients in this study were younger than previous studies. The most common aberrations in chromosomes are trisomy 8, followed by numerical changes in chromosome 5 and 7. The median in total patients was 21 months with many patients received intensive treatment, including HSCT in 45.2% of patients. We also confirmed that patients with poor-risk karyotypes had very poor median OS of 7 months. Therefore, we suggest that although erythroid/myeloid subtype is similar to the MDS with excess blast, treatment decision might be carefully considered according to the karyotype risk.

PB1685

PREGNANCY ACCUMULATES UNFAVORABLE MOLECULAR GENETIC AML AND SHOULD BE CONSIDERED AS A POOR PROGNOSTIC FACTOR

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Background: Acute myeloid leukemia (AML) during pregnancy – is a rare clin-