■ Non-Hodgkin's Lymphoma

OP-001 Abstract Referance: 88

EXOSOMAL DNA FROM PLASMA OF PATIENTS WITH DLBCL: COMPARISON DNA METHYLATION PATTERNS OF EZH2-TARGET GENES OF EXOSOMES AND MATCHING PRIMARY TUMOR TISSUE

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Diffuse Large B-Cell Lymphoma (DLBCL) is the most common type of aggressive lymphoma, and accounts for approximately 30-40% of non-Hodgkin's lymphomas. The pathogenesis of DLBCL is a highly complex multistep process which is not fully understood. It is well known that exosomes derived from cancer cells are able to transfer important modulators for tumor formation, progression and spread. The current study was designed to assess whether the tumor specific epigenetic alterations detected in the primary tumor may be found in plasma exosomes of patients with DLBCL. In this respect, we focused on *EZH2*-target genes including *CDKN1A*, *CDKN1B*, *CDKN2A*, and *CDKN2B*.

This study included 21 DLBCL patients who did not recieve chemotherapy and 21 age-matched healthy controls. Exosomes were isolated from blood plasma by ultracentrifuge-based protocol and verified by electron microscopy, total protein concentration and western blot. After DNA isolation from the exosomes and primary tumor tissue samples, methylation-specific PCR was used to determine methylation status of the target genes. DNA sequencing was used to determine the presence of mutation in *EZH2*.

In concordance with the primary tumors, unmethylated *CDKN1A* and *CDKN1B* DNAs and methylated *CDKN2A* and *CDKN2B* DNAs were determined in the exosomes isolated from DLBCL patients. In addition to, *EZH2*Y641 mutation was not detected in both exosome samples and primary tumor samples counterparts.

To our best knowledge, this is the first study to show that plasma exosomes include DNA fragments which is in concordance with primary tumors in DLBCL. We thought that plasma exosomes preferentially packed both methylated *CDKN2A* and *CDKN2B* DNAs in accordance with primary tumor tissues and may be a suitable source to investigate the presence of this dual methylation marker.

Keywords: Diffuse Large B-Cell Lymphoma, exosome, DNA methylationn, EZH2-target genes

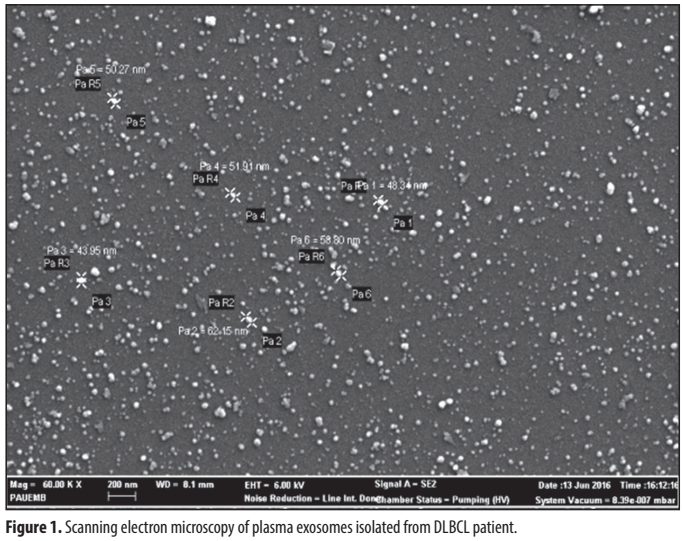

Figure 1. Scanning electron microscopy of plasma exosomes isolated from DLBCL patient.

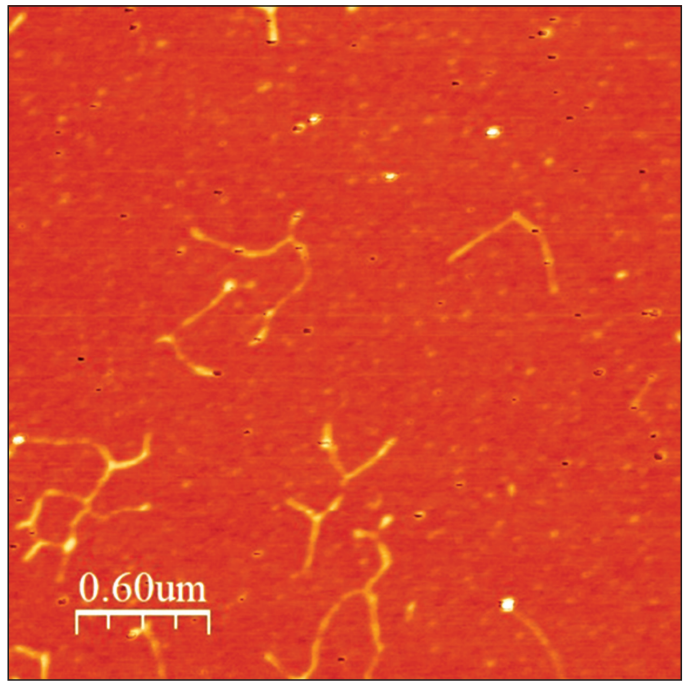

Figure 2. Atomic Force Microscopy image of exosomal DNA. Exosomal DNA was absorbed on a mica surface in the presence of 5 mM Mg2+.

■ Chronic Myeloid Leukemia

OP-002 Abstract Referance : 62

AN ADAPTIVE PHENOTYPIC SHIFT LEADS TO TKI RESISTANCE BY ACQUISITION OF LEUKEMIC STEM CELL-LIKE PROPERTIES IN CML CELLS

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Tyrosine kinase inhibitor (TKI) resistance is a major problem in chronic myeloid leukemia. Phenotype switching has been identified as an escape route for cancer cells. A reversible phenotypic plasticity in tumor cells renders a proportion of cells to be more aggressive and resistant to therapy. To understand the role of cellular plasticity in TKI resistant CML cells, we generated a high dose imatinib-resistant K562 subclone, K562-IR. We've shown that K562-IR cells are not only resistant to imatinib but also to 2nd, 3rd generation TKIs and cytotoxic drugs. Sequencing data revealed that no kinase domain mutations were present. Both K562 and K562-IR showed extensive oncogene amplification, albeit there was no difference between the two. In addition, no difference in BCR-ABL mRNA expression levels was observed. No difference in the inhibition of p-BCR-ABL, p-STAT5, p-CrkL and PDGF signaling between K562 and K562-IR cells, following imatinib treatment was observed; indicating imatinib is sufficiently active and functional in both cell lines. K562-IR cells are capable in growing in monolayers, proliferate slower than their parental counterparts and are resistant to doxorubicin-induced senescence. Unlike its parental cell line, TKI resistant K562-IR cells form tumor spheroids, express high levels of E-cadherin, caveolin-1, CD44 and decreased β-catenin.

Expression of CD45 is significantly reduced in resistant cells; suggesting that K562-IR cells are gradually drifting away from their hematological origin. Cell surface expression of CD33, CD146, and CD65 were also decreased.

CD34 and CD38 are markers for both HSC and LSCs. K562 and K562-IR cells are negative for CD38 in repeated experiments. CD34 expression was either negative or displayed low positivity (1-4%) and comparable in both cell line. Their CD34-/CD38- and decreased β-catenin expression deviates from the accepted LSC phenotype, albeit high CD44 expression.

In CML, we propose that cells undergone "adaptive phenotypic shift" will display different transcriptional frameworks; some partially, others fully compatible with the LSC/CSCs phenotype. Neoplastic cells have the potential of phenotype switching, however only a minority succeeds at any given time. Subset of cells defined as LSC/CSCs may be transient states rather than entities. Recognizing APS has great clinical importance. With LSC/CSC targeted therapies underway, the difference between treating an entity and a spectrum of dynamic reversible states will have conclusive effects on the outcome. APS also needs to be investigated in the context of leukemic cell dormancy and recurrence after withdrawal of TKI treatment in CML. The achievement of long-term clinical responses in targeted therapy will depend on successful targeting of these adaptive phenotypic modulations in cancer cells.

Keywords: Chronic myeloid leukemia, drug resistance, cancer stem cell, transcriptional instability, adaptive phenotypic shift

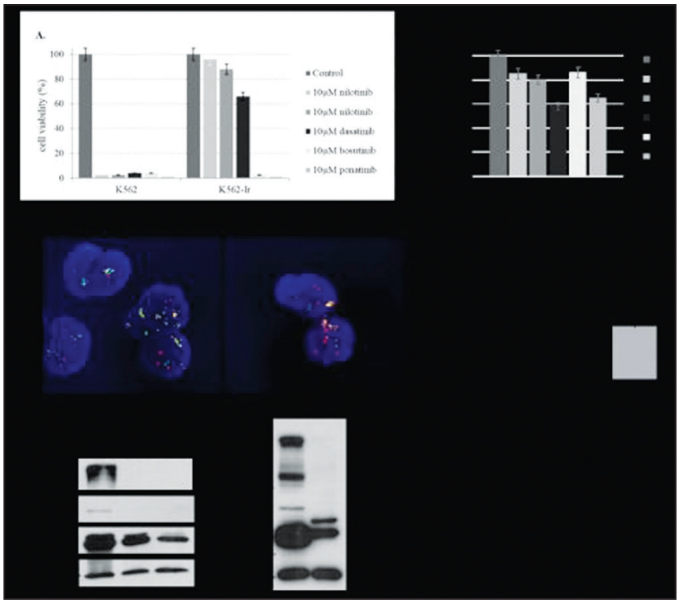

Figure 1. K562-IR cells are resistant to TKIs and do not conform to known TKI resistance mechanisms. A. Cell viability of K562 and K562-Ir cell treated with 10μM TKIs B. Cell viability of K562-IR cells treated with Cmax (daily clinical dose) concentrations. Flow cy

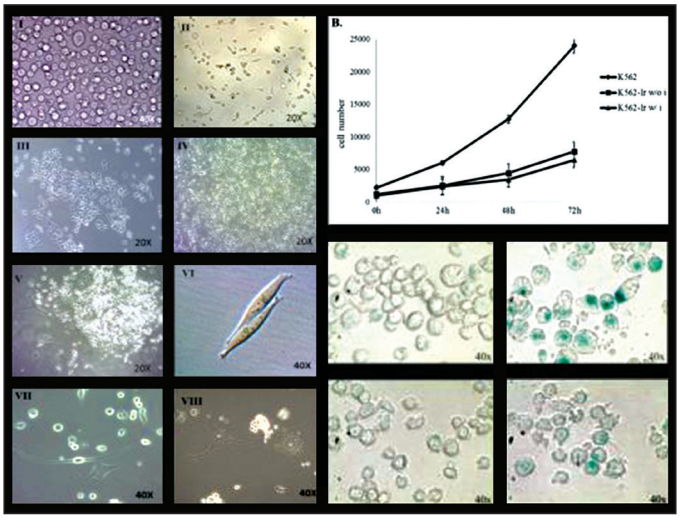

Figure 2. Cellular morphology and proliferative properties of K562-IR cells. A. K562 parental cells (I). K562-IR cells 24h day after of a new passage. A few adherent cells are observed. (II). Proliferation of adherent K562-IR cells (III). Monolayer of K562-IR cell

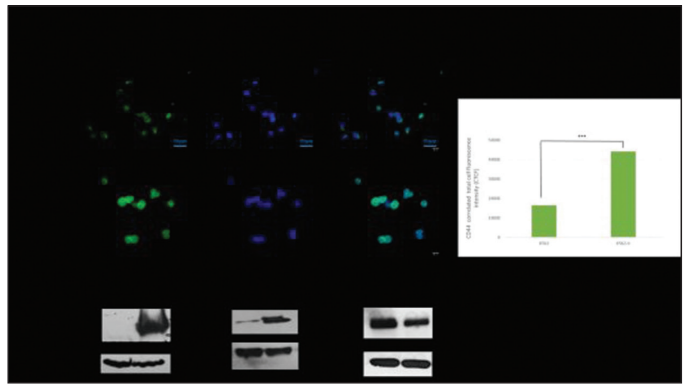

Figure 3. Protein expressions of CD44, Caveolin-1, and B-catenin in K562 and K562-IR cells. A. CD44 immunofluorescence staining. DAPI was used for nuclear visualization. Total corrected cellular fluorescence (TCCF) intensity of CD44 immunofluorescence images (righ)

■ Chronic Myeloid Leukemia

OP-003 Abstract Referance : 98

LONG NONCODING RNA HOTAIR IS A NEW POTENTIAL BIOMARKER FOR CHRONIC MYELOID LEUKEMIA (CML) NOT FOR ACUTE MYELOID LEUKEMIA (AML) IN TURKISH PATIENTS

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Homeobox Transcript Antisense Intergenic RNA (HOTAIR) is a long non-coding RNA that is reported to be more expressed in various cancers in humans compared to non-cancerous adjacent tissues in recent studies. However, little is known about the role of *HOTAIR* in acute myeloid leukemia (AML) and chronic myeloid leukemia (CML). In this study, we aimed to investigate the relationship of *HOTAIR* and *HOXD* genes with leukemia such as AML and CML. Expression levels of *HOXD8, HOXD9* and *HOXD11* genes from *HOXD* genes and *HOTAIR* were determined from peripheral blood samples of 30 AML and 30 CML patients and 20 healthy controls as control group by Real Time PCR method. The expression levels of *HOXD9* gene in the AML patients was significantly lower than the control group ($p < 0.05$). There was no statistically significant difference in the expression levels of *HOTAIR* and *HOXD11* and *HOXD8* genes in the AML patients when compared to the control group ($p > 0.05$). In the newly diagnosed CML patient group; there was a statistically significant increase in the expression level of the *HOTAIR* gene compared to the control group ($p<0.05$). The expression levels of *HOXD9* and *HOXD11* genes in CML patient groups were found to be statistically significantly lower than control group ($p<0.05$).

This study was supported by Erciyes University Scientific Research Projects Unit as TYL-2016-6245 project and Erciyes University Ethics Committee received approval.

Our study showed that *HOTAIR* is not a biomarker in the diagnosis of AML and *HOTAIR* expression is not significantly correlated with the clinicopathological prognostic characteristics of AML. There is still a need for more extensive studies on the level of *HOTAIR* expression in patients with AML.

As a result; It can be said that the *HOTAIR* gene is oncogenic by suppressing the expression of *HOXD9* and *HOXD11* genes in CML patients. In addition, our study, clinical route and drug use of CML patients were followed. Expression level of *HOXD11* and *HOXD8* genes were found to be significantly lower in patients with drug exchange ($p > 0.05$). No significant difference was observed when the expression levels of the other genes measured at the time of diagnosis of CML patients were compared between patients who responded to treatment and those who did not and were resistant to

imatinib. *HOTAIR* may be a potential biomarker in the diagnosis of CML and its prognostic effects in CML patients should contine to be investigated.

HOTAIR gene expression of the CML group was higher than the AML group (p <0.05). The *HOTAIR* gene expression level in the patient group (AML-CML) was found to be significantly higher than the control group (p = 0.032). According to our findings, the increase in *HOTAIR* expression may be play an important role in the development of leukemia. This study provides a new insight into the relationship of *HOTAIR* with HOXD genes in leukemia; however, the molecular mechanisms of *HOTAIR* and HOXD genes should continue to be elucidated in the development and prognostic significance of CML and AML.

Keywords: HOTAIR. lncRNA. HOXD. AML. CML

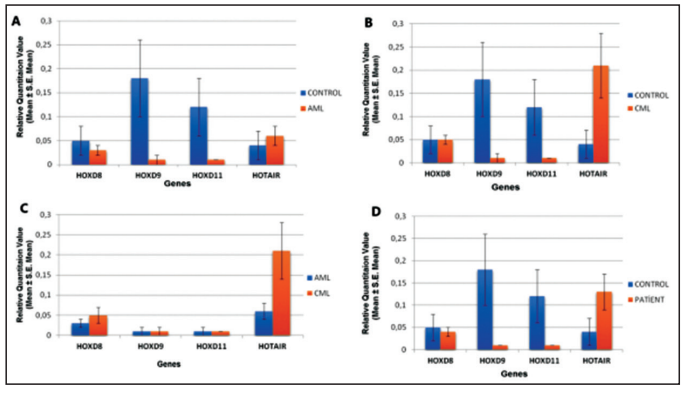

Figure 1. Comparison of Mean Values of Expression Levels of Target Genes Among Control, CML and AML Patient Groups

■ Acute Lymphoblastic Leukemia

OP-004 Abstract Referance : 145

WHOLE GENOME EXPRESSION PROFILING AT DIAGNOSIS PREDICTS RELAPSE IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Aziz Sancar Institute of Experimental Medicine, Department of Genetics, Istanbul University

Acute lymphoblastic leukemia (ALL) is the most common malignancy seen among children accounting for 30% of pediatric cancers. Despite the overall favorable treatment outcome, relapse remains the major clinical challenge in childhood ALL.

In our study, we aimed to identify relapse specific gene expression profile in diagnostic ALL. Raw microarray data (Affymetrix HG-U133_Plus_2) of 351 childhoods ALL samples obtained at diagnoses were retrieved from public databases; four cohorts from GEO database (GSE13576, GSE18497, GSE28460, GSE46170) and one cohort from ArrayExpress database (E-MTAB-2305). Diagnostic samples were labeled either as early relapse or non-relapse feature. Raw CEL. files were used for background correction and RMA normalization. ArrayQualityMetrics was used for QC analyses. ComBat and Harman packages were separately used for batch effect removal and gPCA and pvca packages were used for batch extent and the efficacy of its removal. *Limma* package was used for differential gene expression analysis.

Out of total 351 samples 40 were excluded due to the quality issues. Using an adjusted *p value <0.05* we defined a signature 243 probes that were differentially expressed between diagnosis with non relapse future and diagnosis with relapse feature. This list of significant probes were submitted to DAVID database and Hematopoietic cell lineage (Benjamini corrected *p value 2e-6*), Cell adhesion molecules (*2.6e-6*), B cell receptor signaling pathway (*2.3e-5*), Primary immunodeficiency (*3.6e-5*), Antigen processing and presentation (*4e-5*) and T cell receptor signaling pathway (*2.4e-4*) were seen among others as significantly enriched pathways. Same filter were applied only for B-ALL subtype and 44 genes were found significant. Functional annotation revealed enrichment in genes related to translation initiation (*p value = 7.3e-4*), focal adhesion (*2.1e-3*), extracellular exosome (*3.7e-3*), ribosome (*2.2e-2*) and rRNA processing (*3.2e-2*) in B-ALL samples. In total 95 probes have been found differentially expressed in T-ALL (p*<0.01*) and functional annotation revealed genes related to RNA splicing (*p value = 1.8e-2*), mRNA processing (*2.2e-2*), transcription regulation (3.5e-2), cell cycle (4.1e-2).

Microarray data gives us great opportunity to get high throughput data in a single experiment. But microarray data usually contain inherent technical challenges, which should be handled carefully during normalization and batch removal steps. Herein, we have analyzed an ALL cohort consisting of data obtained from 5 different study groups. Four out of five cohorts had significant variation stemming from scan data (year) of samples, which shows that batch effect may present itself not only when conducted in different centers but also within a single center. Differential gene expression analysis of good and poor therapy responded ALL patients provides an opportunity to discover the biological pathways that may contribute to drug resistance. Our results examining confirm many of earlier findings, but also offer new insight into the relapse.

Keywords: Acute lymphoblastic leukemia, expression array, relapse

■ Acute Lymphoblastic Leukemia

OP-005 Abstract Referance : 97

A NOVEL MARKER CD317 IN PATIENTS WITH CD34 NEGATIVE B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: CD317 was identified in normal B-cells and B-cell malignancies like multiple myeloma and chronic lymphocytic leukemia. However, CD317 is barely detectable in B-cell acute lymphoblastic leukemia. In this study, we investigated the relationship between the presence of CD317 and other markers in flowcytometry in newly diagnosed B- cell acute lymphoblastic leukemia (B-ALL) patients.

Methods: 69 patients age of between 0 and 93 years were included in the study diagnosed with B-ALL betweenJanuary 2017 and December 2018. Demographic features and flow cytometric data of patients were retrospectively evaluated. CD317 and other markers used in diagnosis investigated in bone marrow and peripheral blood samples with ten-color flow cytometry. For comparison, chi square and fisher exact test were used for the nominal data and Mann Whitney U test for the non-nominal data in SPSS 15.0 statistics program. 20% was the cut off for CD34 and CD317 to be considered positive in blastic cells.

Results: In 75% of patients (n=52) ALL blast were CD34 positive and in 25% of patients (n=17) blast were CD34 negative. No statistical difference was found in terms of gender, sample type, leukocyte count, lymphocyte count, hemoglobin and platelet count between CD34 positive and negative groups. However, $CD34^{negative}$ patients tended to be younger. Median age of $CD34^{positive}$ patients and $CD34^{negative}$ patients were 29 years (range: 2-93 years) and 15 years (range: 0-65, respectively (p = 0.08), (table 1). In patients with $CD34^{negative}$ blast, these cells were also found to have a higher rate of CD45 expression, in which the association of TDT, CD19, CD10 and CD19 expression and the rate of CD79a expression were lower (Table 2). CD317 expression rate was 26% in ALL blast. Moreover, when expression of CD34 and CD317 in ALL blast were evaluated together, $CD34^{-}/CD317^{+}$ cells were obtained in more than half of patients and $CD34^{+}/CD317^{+}$ cells in only 17% of patients. The result was statistically significant (p=0,009), (Table 3).

Discussion: In our study CD317 expression of blast was observed in ¼ of B-ALL patients However, when $CD34^{negative}$ blasts were examined in detail, CD317 expression was found in more than half. Our results suggest that CD317 expression might be of diagnostic significance for B-ALL particularly

in CD34 negative blastic cells. CD317 could be used as a new marker for minimal residual disease detection in B-ALL and our study on the prognostic significance of CD317 for B-ALL is ongoing.

Keywords: CD317, B-Cell Acute Lymphoblastic Leukemia

All tables of the study

Table 1 Demographic features of patients at the time of diagnosis

	CD34+	CD34-	P value
Gender, n (%)			
• female	28 (54)	9 (53)	1.0
• male	24 (46)	8 (47)	
Sampletype, n (%)			
• peripheralblood	22 (42)	4 (24)	0.25
bone marrow	30 (58)	13 (76)	
Count of leukocytes	23.2X10³/µl (14.4X10³/µl -774 X10³/µl	15.9 X10³/µl (28 X10³/µl–258 X10³/µl)	0.75
Count of lymphocyte	15 X10³/µl (0.97 X10³/µl -647 X10³/µl)	7.5 X10³/µl (2.4 X10³/µ-117.66X10³/µl)	0.38
Hemoglobin	8,8 g/dl (2,4-13,2)	8,0 g/dl (3,6-11,1)	0.27
Count of thrombocyte	62 X10³/µl (8 X10³/µl -284 X10³/µl)	37X10³/µl (17X10³/µl -181X10³/µl)	0.18
Age, median (range)	29 years (2-93)	15 years (0-65)	0.08

Table 2 Flowcytometry data of patients at the time of diagnosis

	CD34+	CD34-	P değeri
CD 45 ratio, median (range)	9 (0-99)	93 (0-100)	0.03*
CD 38 ratio, median (range)	81 (0-98)	86 (3-96)	0.55
TDT ratio, median (range)	91 (0-98)	49 (0-99)	0.006*
CD10 with CD19 ratio, median (range)	88 (0-98)	57 (0-99)	0.02*
CD19 ratiomedian (range)	93 (0-99)	85 (14-99)	0.02*
CD20 ratio, median (range)	2 (2-95)	7 (0-98)	0.16
CD22 ratio, median (range)	63 (0-97)	58 (0-98)	0.64
CD79a ratio, median (range)	94 (0-99)	81 (39-99)	0.005*
CD9 ratio, median (range)	95 (56-99)	83 (40-90)	0.15
MPO ratio, median (range)	0 (0-3)	0 (0-59)	0.17
CD15 ratio, median (range)	0 (0-93)	7 (0-86)	0.006*
CD33 ratio, median (range)	0 (0-91)	0 (0-92)	0.67
CD13 ratio, median (range)	0 (0-94)	0 (0-50)	0.75
CD58 ratio, median (range)	99 (80-100)	95 (3-99)	0.15

Table 3 The relationshipbetween CD317 and CD34

	CD34+	CD34-	P value
CD317, n (%)			0.009*
• positive	9 (17)	9 (53)	
• negative	43 (83)	8 (47)	

■ Chronic Myeloid Leukemia

OP-006 Abstract Referance : 59

EPIDEMIOLOGY OF CHRONIC MYELOID LEUKEMIA IN AZERBAIJAN

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Background: Chronic myeloid leukemias (CML) widespread throughout the world, with certain differences in climatic and geographical zones, among different social and ethnic groups of the population. The study of epidemiological data is necessary to assess patients morbidity, mortality and survival, to monitor and determine factors affecting them. Epidemiological studies can be used to organize and improve the hematology service in the country.

Aim: The purpose of this study is to study the epidemiological features of CML in Azerbaijan.

Materials and methods: 766 CML patients diagnosed between 2008 and 2017 were researched. The distribution of CML patients by sex, the age groups at the time of diagnosis, economic-geographical and administrative regions of Azerbaijan were calculated. The incidence, prevalence, mortality and overall survival rates of CML patients were analyzed. Additionally, seasonality in the diagnosis of CML was evaluated. P values calculated from chi square using the software IBM SPSS.

Results: As results of our study it was determined that CML is more common in women than in men (respectively 54% and 46%). Median age is 49. Diagnose frequency is highest among the age group 50-59 (1.96 per 100,000), 40-49 (1.65), 30-39 (1.26). The analysis of epidemiological indicators over the period of 2008–2017 showed that the incidence of the disease in the Azerbaijan was increasing. The lowest incidence of CML was noted in 2008 (0.31), the highest was recorded in 2016 (1.01).

Mortality increased from 0.57 (per 100,000) in 2008 to 0.163 in 2017. However, in recent years, there has been not only a stabilization of this indicator and its decrease in 2017 compared to 2016. In connection with the latest advances in the treatment of CML, the response to therapy has changed dramatically. The overall survival in our patients receiving tyrosine kinase inhibitors (TKI) after 10 years was 64%, while the survival of patients who did not receive TKI after 6 years was only 4%. Distribution of CML patients by economic-geographical regions of Azerbaijan, the highest incidence is detected in east side, precisely in Absheron peninsula (10.6 per 100,000) and the lowest is shown in west side, Ganja-Gazakh (5,57). The result of seasonal characteristic of CML shoved that 23.5% of patients diagnosed in autumn, 21.5% in winter, 29.6% in summer and 25.4% in spring. However, seasonal differences were not statistically significant (χ^2=5.3463, p=0.1481).

Conclusion: Although there has been an increase in incidence rates over the study period (2008-2017), it is encouraging that as a result of the use of TKI in the treatment of patients, the survival rate of patients has significantly increased. The results obtained can be used for comparative studies and improvement of specialized medical care for CML patients.

Keywords: Leukemia, Chronic Myeloid, epidemiology.

■ Non-Hodgkin's Lymphoma

OP-007 Abstract Referance: 155

RETROSPECTIVE ANALYSIS OF 149 UNSELECTED PATIENTS WITH MANTLE CELL LYMPHOMA CONFIRMS PROGNOSTIC RELEVANCE OF MIPI: SINGLE CENTER EXPERIENCE

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Introduction: Mantle cell lymphoma (MCL) is an uncommon subtype of non-Hodgkin lymphoma with distinguished clinical, biologic, and molecular characteristics. The MCL-International Prognostic Index (MIPI) incorporates age, EGOC performance status, normalized LDH level and WBC and has improved discriminatory power. The aim of this retrospective single-center study was to evaluate the clinical characteristics and response to treatment of patients with MCL.

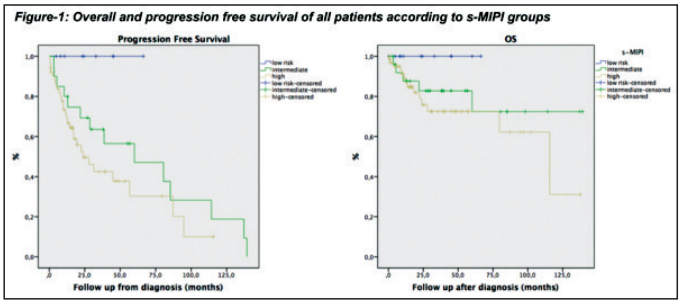
Methods: This single center retrospective study included 297 adult patients diagnosed with MCL between December 2005 and May 2018. The diagnosis of MCL was rendered in accordance with the later World Health Organization (WHO) classification. Outcome was determined as response to treatment, progression free survival (PFS) and overall survival (OS) by Kaplan-Meier analysis using SPSS (IBM SPSS Statistics 21; IBM Corp., Chicago, IL) statistical tool kit. We also compared the PFS and OS according to simplified MIPI (s-MIPI) index.

Results: All clinical data were available in 149 cases. There were 38 (26%) female and 208 (74%) male patients. The median age at diagnosis was 66 years (range, 31-93 years). The median time of follow-up was 14.5 months (range, 3-139.3 months). Bone marrow and extra-nodal involvements was observed in 64 patients (43.8%) and 23 patients (15.7%), respectively. The median s-MIPI was 6 points (range 2-11). Most patients were in the high-risk group (62.2%). Induction chemotherapy was administered in 128/146 patients. Two patients deceased after diagnosis. One hundred and fifteen out of 146 patients (78.8%) were treated with a combination of chemotherapy and anti-CD20 monoclonal antibody rituximab. One elderly patient received Rituximab immunotherapy only. The majority (56.5%) of the patients received CHOP with rituximab as induction chemotherapy. Thirty-one patients underwent ASCT. In total 40 patients achieved complete remission (CR) with an overall response rate of 63.9% after the induction therapy. During follow up, 20 relapses and 28 deaths were noted. Infection was thesss most common cause of death (50%). Following ASCT, OS was significantly

improved; estimated median OS in transplant cohort was 115.7 months vs. 60 months compare with non-transplant group (p=0.013). According to the long-rank test, estimated 5-year OS was not significantly different between intermediate-risk and high-risk s-MIPI categories (72.4%±1.2% vs. 72.6%±0.7%; p=0,202). Estimated 5-year PFS was significantly different between intermediate-risk and high-risk s-MIPI cohorts (47.1%±1.3% vs. 33%±10.3%; p=0,05). Among the transplanted patients, there is no differences between the OS of s-MIPI groups (p=0.952). No patient died or progressed in the low-risk group.**Conclusion:** We have confirmed the validity of the MIPI and simplified MIPI for the prognosis of patients with MCL even in the era of rituximab. The general results of both indexes are fully comparable, facilitating the broad application of s-MIPI as a simple bedside prognostic tool.

Keywords: Mantle cell lymphoma, The MCL-International Prognostic Index (MIPI)

Figure-1: Overall and progression free survival of all patients according to s-MIPI groups



■ Other

OP-008 Abstract Referance: 69

VANCOMYCIN RESISTANT ENTEROCOCCI COLONIZATION, PREDISPOSING FACTORS FOR INFECTION AND PROGNOSTIC FACTORS IN PATIENTS WITH FEBRILE NEUTROPENIA

Tugcan Alp Kirkizlar[1], Halis Akalin[2], Onur Kirkizlar[3], Ridvan Ali[4]

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Introduction: Vancomycin resistant enterococci (VRE) colonization is mostly found in high risk units like haemato-oncology units. Vancomycin resistant enterococci colonization has an increasing risk of VRE infections, mortality and longer hospitalization. In the studies VRE infection rate changes between 0-45% in colonized patients. Some risk factors were determined such as advanced age, severity of disease, prolonged hospitalization, gastrointestinal surgery, transplantation, exposure to medical devices and broad spectrum antimicrobial agents for VRE infection.

The aim of this study is to analyse epidemiological data and to evalute possible risk factors associated with VRE infection and mortality in colonized acute leukemia patients with febrile neutropenia.

Methods: Two hundred and forty adult acute leukemia patients with febrile neutropenia (FN) who colonized with VRE were included to the study between January 2010-January 2016 in Uludag University Medical Faculty Hematology Clinic. We used open source software R 3.4.4, revision number 74408 for statistical analysis. For continuous variables, we provide the mean and standard variation. For comparing continuous variables, we used Mann-Whitney-Wilcoxon and t tests. For comparing categorical variables, we used the χ^2 test or Fisher exact test, as seen appropriate.

Results: Two hundred and seventeen patients were in colonized group while 23 were in infected group. *Enterococcus faecium* was isolated in all patients. Mean age was 47 years (median 54) in infected group and 43 years (median 45) in colonized group (p= 0.155). Female/male ratio were 1,55 and 0,63 in infected and colonized groups respectively (p= 0.066).Active disease was present in 82.1% in colonized group while 86.9% in infected group (p= 0.774). Demographic, epidemiological and clinical characteristics of the patients were shown in Table 1. The infection rate was found 9,58%. The distrubition of infections were 15 (65.2%) blood stream, 3 (13%) skin and soft tissue, 2 (8.7%) urinary infections and others (13.1%). In the multivariate logistic regression analysis, advanced age, previous colonization, exposure to invasive procedures, coinfection and duration of VRE positivity were found as independent risk factors for VRE infection in VRE colonized patients. Among all patients 86.25% survived and 13.75% died. In the infected patients 47.9% survived and 52.1% died while 90.3% survived and 9.7% died in colonized patients. The all cause of mortality rate between groups is statistically significant (p= <0.001).

Discussion: Vancomycin resistant *enterococcus*is considered as a pathogen bacteria causing an infection which result in subsequently morbidity and mortality especially in high risk patients such as neutropenic from haematology and oncology departments. The VRE colonized cancer patients who had FN tend to VRE infection much more than the general hospitalized patients. In the studies, infection rate in colonized patients seem higher than ours. Some risk factors were revealed about transition from colonization to infection similar to our study. Worth et al. demonstrated all cause of mortality 21.4% in patients with VRE infected while 52.1% in our study. The clinical approach to VRE infected patients should be revised due to higher mortality rates. We need risk assessment models which defining high risk patient groups for VRE colonization and infection and empirical or treatment options to avoid morbidity and mortality.

Keywords: Vancomycin-Resistant Enterococci, Leukemia, Febrile Neutropenia

Table 1. Demographic, epidemiological and clinical characteristics of the patients and risk factors

	Infected (n = 23)	*Colonized (n = 217)*	*P Value Mann-Whitney-Wilcoxon*	*P Value t-test*	*P Value χ2 or Fisher exact*
Age	Mean = 47.13 St. Dev. = 14.86 Median = 54	Mean = 43.92 St. Dev. = 14.01 Median = 45	0.155	0.331	
Gender (M/F)	M= 9 (39.2%) F = 14 (60.8%)	M = 133 (61.3%) F = 84 (38.7%)			0.066
Diagnosis	ALL = 5 (21.7%) AML = 18(78.26%)	ALL = 51(23.5%) AML = 166(76.5%)			0.999
Active/Remission	Active = 20(86.9%) Remission = 3 (13.1%)	Active = 178 (82.1%) Remission = 39 (17.9%)			0.774
Previous hospitalization	0 = 13 (56.5%) 1 = 3 (13%) 2 = 2 (8.75%) 3 = 3 (13%) ≥4 = 2 (8.75%)	0 = 104 (47.9%) 1 = 51 (23.5%) 2 = 29 (13.3%) 3 = 23 (10.7%) ≥4 = 10 (4.6%)			0.574
Previous colonization status	Negative = 21 (91.3%) Positive = 2 (8.7%)	Negative= 175 (80.6%) Positive = 42 (9.4%)			0.267
Number of days colonized	Mean = 17.96 St. Dev. = 10.76 Median = 17	Mean = 21.51 St. Dev. = 12.85 Median = 19	0.183	0.151	
Empirical antibiotics for FN (in the last week before evaluation of the colonization)	Yes = 21 (91.3%) No = 2 (8.7%)	Yes = 194 (89.4%) No = 23 (10.6%)			0.999
Exposure to vancomycin/ daptomycin/ linezolid duringcolonization	None =13 (56.5%) D = 0 V =10 (43.5%) D & L = 0 V & L = 0	None = 128 (59%) D= 3 (1.4%) V = 82 (37.8%) D& L = 2 (0.9%) V & L= 2 (0.9%)			0.913
Exposure to broad spectrum antibiotics after colonization (modification of treatment after colonization)	Yes = 19 (82.6%) No = 4 (17.4%)	Yes = 113 (52%) No = 104 (48%)			0.007
Mucositis (oral mucositis or diarrhea)	No = 13 (56.5%) Yes = 10 (43.5%)	No = 128 (59%) Yes = 89 (41%)			0.995
Central venous catheter	Yes = 13 (56.5%) No = 10 (43.5%)	Yes = 143 (65.9%) No = 74 (34.1%)			0.505
Invasive procedures	No = 17 (74%) Yes = 6 (26%)	No = 212 (97.7%) Yes = 5 (2.3%)			0.0001
Acute kidney injury	No = 22 (95.7%) Yes= 1 (4.3%)	No = 179 (82.5%) Yes = 38 (13.5%)			0.138
Duration of neutropenia (days until colonization)	Mean = 14.96 St. Dev. = 16.52 Median = 11	Mean = 20.86 St. Dev. = 13.98 Median = 19	0.005	0.110	
Coinfection	Yes = 15 (65.2%) No = 8 (34.8%)	Yes = 199 (91.7%) No = 18 (8.3%)			0.001
Neutrophil counts while VRE(+)	<0,5x 109 /L = 22 (95.7%) 0,5-1x 109 /L =0 1-1,5x 109 /L = 0 >1,5x 109 /L = 1 (4.3%)	<0,5x 109 /L = 135 (62.2%) 0,5-1x 109 /L = 7 (3.2%) 1-1,5x 109 /L = 17 (7.8%) >1,5x 109 /L = 58 (26.8%)			0.0001
VRE (+) days	Mean = 34.74 St. Dev. = 32.34 Median = 21	Mean = 16.81 St. Dev. = 14.96 Median = 14	0.001	0.015	
≥3 Weeks VRE (-)	No = 23 (100%) Yes = 0	No = 208 (95.9%) Yes = 9 (4.1%)			0.0001
Time between arrival to hospital and colonization	Mean = 17.96 St. Dev. = 10.76 Median = 17	Mean = 21.51 St. Dev. = 12.85 Median = 19	0.183	0.151	

M: male, F: female, AML: acute myeloid leukemia, ALL: acute lymphoid leukemia, FN: febrile neutropenia, VRE: vancomycin-resistant enterococcus, D: daptomycin, V: vancomycin, L: linezolid

■ Acute Myeloid Leukemia

OP-009 Abstract Referance: 157

LEUKAPHERESIS REDUCES 4-WEEK MORTALITY IN ACUTE MYELOID LEUKEMIA PATIENTS WITH HYPERLEUKOCYTOSIS - A RETROSPECTIVE STUDY FROM A TERTIARY CENTER

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Introduction: Hyperleukocytosis (HL) is defined as the clinical condition when the white blood cell (WBC) count is above 100 000/mm^3 in peripheral blood and the reported incidence of HL is between 5 and 20% in acute myeloid leukemia (AML). The effect of leukapheresis on early mortality data is scarce. The aim of this study was to investigate the effect of leukapheresis on early mortality of AML patients with HL.

Patients &Methods: From January 2005 through October 2017, data from 70 patients with AML who were eligible for leukapheresis were evaluated. All these data were obtained from the Ankara University Faculty of Medicine Center for Therapeutic Apheresis and written informed consent was signed according to our institution regulations. All leukapheresis procedures were performed according to the institutional standard operating procedures after informed consent. Leukapheresis was performed with a continuous-flow blood cell separator (COBE Spectra; TerumoBCT, software version 7.0) via central venous access. The leukapheresis procedures were continued on a daily basis until clinical improvement was determined. Early mortality was defined as death within the first 15 days of leukapheresis.

Results: The study cohort consisted of 70 (36 male/33 female) newly diagnosed AML patients who had presented with HL and/or symptoms of leukostasis and underwent leukapheresis. The median age was 52 years (range, 4–86 years). The median WBC counts at diagnosis was 179.2x10^9/L (range, 56.5-558.0x10^9/L). The majority of patients, 88.6% (n=62) had WBC count ≥100x10^9/L. The majority of patients had symptoms of pulmonary leukostasis. A total of 140 leukapheresis cycles were performed among the 70 AML patients. The median number of leukapheresis cycles was 2 (range, 1–7). The median initial WBC was 179.2×10^9/L, which reduced to 121.7x10^9/L after the first leukapheresis. Eleven of the seventy patients had died by the time of analysis. Seven patients (10%) died within two weeks after leukapheresis commenced. Among the 7 patients, one patient was treated with induction chemotherapy and the remaining received palliative and supportive care. The main cause of early death was respiratory failure. The mean overall survival for all patients was 112±17 months (95% CI 78–145 months) (Figure). The median overall survival for patients who achieved complete all-cause 2-week mortality rate was 10% (7/70 patients) and the all-cause 4-week mortality rate was 12.8% (9/70 patients).

Conclusion: Leukapheresis is effective and safe procedure in reducing the peripheral blood leukocytes and leukemia blasts. Furthermore, high initial response rates in a subgroup of newly diagnosedAML patients fit to receive intensive chemotherapy suggest that leukapheresis could be beneficial in reducing the complications associated with hyperleukocytosis until systemic intensive chemotherapy commences.

Keywords: acute myeloid leukemia, hyperleukocytosis, leukapheresis

■ Other

OP-010 Abstract Referance: 133

HODGKIN LYMPHOMA IN THE ELDERLY: A RETROSPECTIVE MULTICENTER STUDY BY TURKISH SOCIETY OF HEMATOLOGY, LYMPHOMA ACADEMY

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Introduction: Hodgkin Lymphoma in elderly is described as the disease of patients over the age of 60. Treatment response of this population has been shown as being worse than the young population, due to both disease characteristics and patient related factors. In this study, data from elderly population was analyzed retrospectively.

Methods and Results: 52 patients from 4 centers were identified and reviewed. Table 1 shows the characteristics of these patients. The mean age was 69.4 years (range: 60-91 years). 37% of the patients had at least one comorbidity including COPD, DM, hypertension and chronic ischemic cardiovascular disease. 51 of 52 patients had received chemotherapy; 43 of them had ABVD regimen. Overall response (complete +partial) was 73.1%. Eight patients died during treatment (Table 2). Hematologic, neurologic or pulmonary side effects were observed in 57.6% of treated patients. Seventeen of them had therapy modifications while 31% of patients had bleomycin toxicity. The use of G-CSF (11 of 13 patients) was more common in patients who had pulmonary toxicity compared to patients without pulmonary toxicity (p: 0,01). Median survival was not reached, and two-year overall survival was 72.6% (Figure 1).

Discussion: Treatment response and survival of Hodgkin Lymphoma in elderly was lower than expected for this patient group. These results can be explained by the patients being late stage, higher rates of histologically aggressive types, having comorbidities affecting the therapy and the need of treatment modification in most of the patients. Although we had small number of patients, the higher rates of pulmonary toxicity in the G-CSF receivers suggested that the use of G-CSF in elderly population should be with caution. The use of monoclonal antibodies such as Brentuximab can become widespread sooner.

Keywords: Lymphoma, Hodgkin, elder

■ Non-Hodgkin's Lymphoma

OP-011 Abstract Referance: 10

CIRCULATING MICRORNA-125A AS A POTENTIAL SERUM BIOMARKER FOR DIFFUSE LARGE B-CELL LYMPHOMA

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Introduction: Diffuse large B-cell lymphoma (DLBCL) is a highly aggressive disease, and it is the most frequent form of non-Hodgkin's lymphoma. MicroRNAs (miRNAs) are short, non-coding RNA molecules that average 18-22 nucleotides long and act as important posttranscriptional regulators. This presents an opportunity for specific miRNAs to serve as diagnostic and prognostic biomarkers for several malignancies.

Method: Serum samples were collected from DLBCL patients and healthy individuals. We extract total RNA from serum collected from 24 DLBCL patients and 23 healthy individuals and performed reverse transcription. In order to quantify miR-125a levels, Realtime quantitative polymerase chain reaction was used to measure miR-125a levels in serum samples from 24 patients and healthy individuals. The relative expression of serum miRNA in CLL cases was analyzed with the $2^{-\Delta\Delta Ct}$ method, using pooled miRNA from normal controls as the reference.

Results: We found that serum miR-125a expression was significantly over-expressed in DLBCL patients (median expression value 3.71, range: 1.31-231.43) to compare healthy individuals (median expression value 1.921, range: 0.29- 8.53; P< 0.001). Moreover, significant correlations were found between miR-125a overexpression and DLBCL patients' clinical characteristics, including staging and International Prognostic Index (IPI). In addition, DLBCL patients with elevated level of miR-125a have shown significantly shorter overall survival (p<0026) than those with lower miR-125a expression. **Conclusion**: This finding suggests that miR-125a in peripheral blood serum could potentially be used as a clinical biomarker for DLBCL.

Keywords: miR-125a, diffuse large B-cell lymphoma, Prognosis

■ Acute Myeloid Leukemia

OP-012 Abstract Referance: 51

COMPARISON OF CONSOLIDATION STRATEGIES IN ACUTE MYELOID LEUKEMIA: STANDARD CHEMOTHERAPY VS AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Treatment of acute myeloid leukemia (AML) is based on remission induction therapy and several consolidation approaches including standard consolidation regimens such as high dose/intermediate dose Ara-C (HIDAC/IDAC) and allogeneic hematopoietic stem cell transplantation (HSCT) based on risk assessment models, particularly cytogenetics. Autologous HSCT is considered as a feasible option for patients without adverse cytogenetics and HLA-compatible donors. The aim of this study is to compare the efficacy of HIDAC/IDAC regimens and autologous HSCT as consolidation modalities in terms of relapse and overall survival (OS) in AML patients.

Methods: A total of 101 patients [median age: 47(19-79) years; M/F: 51/50] who were diagnosed as AML between in 2002 and 2019 were reviewed in this retrospective study.

Results: After standard 7+3 remission induction therapy, 70 patients (69.3%) continued with consolidation chemotherapy including 3 to 4 courses of HIDAC/IDAC, while autologous HSCT was performed in 31 patients (30.7%) after the first consolidation course. Patient characteristics are summarized in Table 1. All patients were in complete remission before HSCT. G-CSF was used for median 8(1-16) days during stem cell mobilization. Median infused $CD34^+$ cell count was 4.47(2.2-5.86)x10^6/kg. Neutrophil and platelet engraftments were achieved on day 12(9-27) and 13(10-202), respectively. Grade 1(1-3) mucositis was observed during peri-engraftment period. A total of 16 patients (51.6%) had neutropenic fever and 1patient (3.2%) had sinusoidal obstruction syndrome. In chemotherapy group, 22 patients (31.4%) experienced hematological relapse at median 330(60-2190) days after the first remission, 4 of these patients (18.2%) underwent allogeneic HSCT for salvage treatment. A total of 14 patients (45.2%) relapsed at median 225(60-395) days after autologous HSCT and 12 patients (85.7%) underwent allogeneic HSCT in this group. At a median follow-up of 915(30-4470) days, OS was found to be better in autologous HSCT group compared to chemotherapy group without statistical significance [79.2% vs 38.8%, p=0.054] (Figure 1). Leukemia risk status at diagnosis was considered as the only prognostic parameter for OS in Cox regression analysis (p=0.002).

Conclusions: In this study, the superiority of consolidative autologous HSCT was demonstrated in AML patients compared to standard chemotherapy arm, without statistical significance. This favourable issue, despite high and early relapse rates after autologous HSCT, may be explained by the additive positive impact of high percentage of salvage allogeneic HSCT in this group of patients. Furthermore, patients in the chemotherapy arm were relatively older and had more comorbidities compared to HSCT group. As leukemia risk status at diagnosis was indicated to be the only statistically significant factor for OS, the importance of patient-based treatment decisions in newly-diagnosed AML patients should be underlined. Small sample size may be another explanation for statistical inconvenience. Further studies are required in order to standardize consolidation strategies in AML patients.

Keywords: Acute Myeloid Leukemia; Autologous Stem Cell Transplantation; Consolidation Therapy; Prognosis

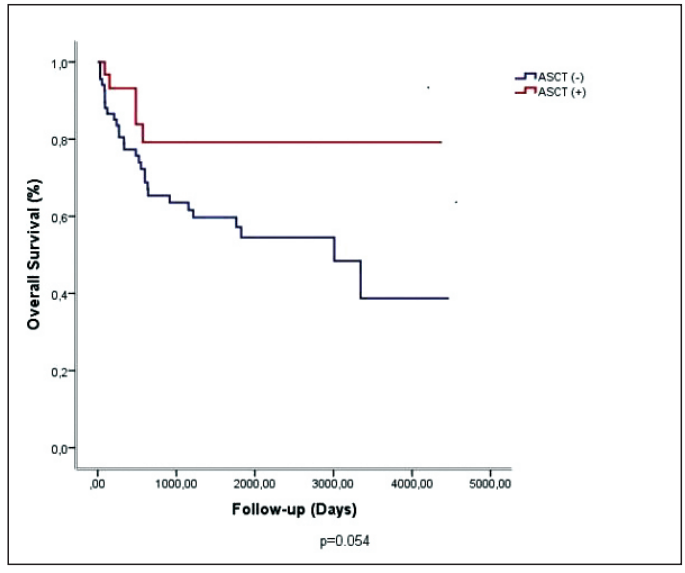

Figure 1. Impact of Autologous HSCT and Standard Chemotherapy on Overall Survival (p=0.054)

Table 1. Patient Characteristics

Age [median(range)] (years)	47(19-79)
Gender [n] (male/female)	51/50
AML Subtype (FAB Classification) [n(%)]	
AML-M0	8(7.9)
AML-M1	13(12.9)
AML-M2	18(17.8)
AML-M4	31(30.7)
AML-M5	9(8.9)
Unclassified	22(21.8)
Risk Status [n(%)]	
Low-risk	12(12.9)
Intermediate-risk	37(39.8)
High-risk	44(47.3)
Extramedullary disease [n(%)]	5(4.9)
CNS involvement [n(%)]	3(2.9)
Time to transplant [median(range)] (months)	95(57-187)
ECOG Performance Status [median(range)]	0(0-1)
Sorror Comorbidity Index [median(range)]	0(0-2)
Mobilization regimen [n(%)]	
HDAC	22(71)
IDAC	7(22.6)
Cy-Etoposid	1(3.2)
G-CSF	1(3.2)
Conditioning regimen [n(%)]	
Cy Bu	30(96.8)
TEAM	1(3.2)
Infused CD34+ Cells [median(range)] (106/kg)	4.47(2.2-5.86)
Neutrophil Engraftment [median(range)] (days)	12(9-27)
Platelet Engraftment [median(range)] (days)	13(10-202)
Sinusoidal obstruction syndrome [n(%)]	1(3.2)
Mucositis Grade [median(range)]	1(1-3)

AML, Acute myeloid leukemia; FAB, French-American-British; CNS, Central nervous system; ECOG, Eastern Cooperative Oncology Group; HDAC, High dose ARA-C; IDAC, Intermediate dose ARA-C; Cy, Cyclophosphamide; G-CSF, Granulocyte colony stimulating factor; Bu, Busulfan; TEAM, Thiotepa, etoposide, cytarabine, melphalan; CD, Cluster of differentiation)

■ Acute Myeloid Leukemia

OP-013 Abstract Referance: 24

POST REMISSION TREATMENT SCORE FOR PREDICTING THE SURVIVAL IN ACUTE MYELOID LEUKEMIA : SINGLE CENTRE EXPERIENCE

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Objective: Post-remission treatment (PRT) in acute myeloid leukaemia (AML) is still a matter of debate. Treatments after first remission may be chemotherapy or allogenic stem cell transplantation (AHSCT) or autologous stem cell transplantation (autoHSCT). The decision to is generally given based on the cytogenetic risk group, but there are also others ,such as age, comorbidity and molecular factors that may affect the outcome of the treatment. A PRT scoring system that included independent prognostic factors such as cytogenetic risk, age, percentage of CD34-positive blasts, *FLT3-ITD* mutant-to-wild-type ratio, and de-novo or secondary AML , has been reported by Priffman et al.

Method: In this single centre trial, 231 patients with AML who were in their first complete remission, treated with AHSCT or chemotherapy were included. Patients were retrospectively classified according to the PRT score. We investigated whether survival after treatment can be predicted by PRT scoring system. The PRT scoring system separated the patients into three groups, such as favourable, intermediate and unfavourable groups.

Results: Overall survival rate after treatment in three groups were significantly different. While there was no difference between transplantation and chemotherapy in the favorable group, our data suggested that stem cell transplantation improved survival in the intermediate and high risk groups.

Conclusion: All risk classification models were only prognostic and could not be used to predict optimum treatments for the different risk categories but the PRT score groups might help physicians to individualise treatment in patient with AML after achieving complete remission. Longer confirmational studies may further elucidate the role of PRT score in patients.

Keywords: transplantation, post,remission,treatment,score

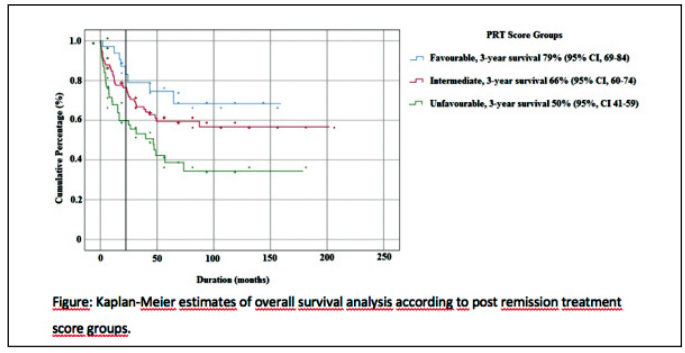

Figure: Kaplan-Meier estimates of overall survival analysis according to post remission treatment score groups.

■ Acute Myeloid Leukemia

OP-014 Abstract Referance: 94

LONG TERM FOLLOW UP OF IDIOPATHIC CYTOPENIA OF UNDETERMINED SIGNIFICANCE (ICUS), CLONAL CYTOPENIA OF UNDETERMINED SIGNIFICANCE (CCUS) TOWARDS MYELODYSPLASTIC SYNDROME (MDS)

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Introduction: Myelodysplastic syndrome (MDS) is defined by World Health Organization (WHO) and International Working Group (IWG)-MDS as not a single but a group of disorders characterized as persistent cytopenia or cytopenias and dysplasia of significant percentage of (≥10%) single or multiple lines in the bone marrow with support of clonal cytogenetic abnormalities. The pre-lesions of MDS, as assimilated with the pre-lesions of multiple myeloma, monoclonal gammopathy of undetermined significance and smoldering myeloma; were defined by pioneers of morphology and persistence of cytopenia (s), persistence of dysplasia, adequate evaluation of clonality are suggested. In this perspective, there are significant number of patients who do not fulfill the diagnostic criteria of MDS, but still, has solely cytopenia or cytopenia and clonality but not MDS. These patients are categorized as Idiopathic Cytopenia of Undetermined Significance (ICUS) who just have persistent cytopenia; Clonal Cytopenia of Undetermined Significance (CCUS) who has persistent cytopenia and a clonality, but this clonality is not suggestive of MDS and Idiopathic Cytopenia of Undetermined Significance (IDUS) who have just dysplasia without cytopenia and no definitive cytogenetics for MDS. In this study, we retrospectively evaluated the data of our patients who have been followed up as MDS but in fact, was either ICUS or CCUS; re-evaluated their cytopenia(s), bone marrow morphology and clonality; combined with a follow up data regarding the potential concern of evolution to MDS and/or AML.

Methods: Data of 300 patients who have been evaluated and regarded as MDS in Trakya University Faculty of Medicine, Department of Hematology were evaluated in a retrospective manner.

Baseline features, including whole blood count, and follow ups, clonal evaluation by conventional cytogenetics are recorded from files. All bone marrow aspirations were re-evaluated by two hematologists and dysplasia observations are recorded and photographed individually.

Results:166 patients were female (55,3%) while 134 were male (44,7%). Mean age was 66,11 years (23-89). Regarding initial presentation, 246 patients were anemic (82%), while 165 patients had leucopenia (55%), 104 patients neutropenia (34,7%) and 161 had thrombocytopenia (53,7%). Morphologic dysplasia was observed in 82 patients (27,3%). 152 patients had no cytogenetical abnormality (50,7%) while 71 patients had MDS related cytogenetical abnormality (23,7%) and 77 patients had clonality but not related with MDS (25,7%). According to initial presentation and findings, 59 patients were regarded as MDS (19,7%), 147 as ICUS (49%), 77 as CCUS (25,7%) and 17 patients (5,7%) were categorized as not MDS-not ICUS-not CCUS, including patients who had dysplasia and not MDS related cytogenetical abnormalities or cytopenia with not MDS related cytogenetical abnormality without dysplasia. Mean follow up duration was 3,04 years (1-11 years). Results regarding follow up were summarized in Table 1.

Discussion: Though regarded as pre-lesions of MDS, ICUS/CCUS/CHIP and all other not-MDS definitive diagnoses should be regarded as distinctive yet, worth to be followed entities.

Keywords: Myelodysplastic sydrome, Cytogenetic

Table 1.

	Initial Evaluation	*First Year*	*Third Year*	*Fifth Year*	*Tenth Year*
CCUS (Anemia)	n=77 62 (80,5%)	n=77 33 (42,9)	n=40 9 (11,7%)	n=25 3 (3,9%)	n=2 none
ICUS (Anemia)	n=147 119 (81%)	n=147 92 (62,6%)	n=47 7 (4,8%)	n=28 4 (2,7%)	n=3 1 (0,7%)
Not-MDS (Anemia)	n=17 12 (70,6%)	n=17 14 (82,4%)	n=6 1 (5,9%)	n=3 none	none none
MDS (Anemia)	n=59 53 (89,8%)	n=59 49(83,1%)	n=30 24 (40,7%)	n=16 4(6,8%)	n=1 none
	Initial Evaluation	First Year	Third Year	Fifth Year	Tenth Year
CCUS (Leucopenia)	n=77 41 (53,2%)	n=77 40 (51,9%)	n=40 16 (20,8%)	n=25 3 (3,9%)	n=2 none
ICUS (Leucopenia)	n=147 88 (59,9%)	n=147 88 (59,9%)	n=47 14 (9,5%)	n=28 4 (2,7%)	n=3 1 (0,7)
Not-MDS (Leucopenia)	n=17 10 (58,8%)	n=17 13 (76,5%)	n=6 4 (23,5%)	n=3 none	none none
MDS (Leucopenia)	n=59 26 (44,1%)	n=59 26 (44,1%)	n=30 8 (13,6%)	n=16 4 (6,8%)	n=1 none
	Initial Evaluation	First Year	Third Year	Fifth Year	Tenth Year
CCUS (Thrombocytopenia)	n=77 37 (48,1%)	n=77 37 (48,1%)	n=40 14 (18,2%)	n=3 none	n=2 none
ICUS (Thrombocytopenia)	n=147 74 (50,3%)	n=147 74 (50,3%)	n=47 17 (11,6%)	n=28 none	n=3 none
Not-MDS (Thrombocytopenia)	n=17 13 (76,5%)	n=17 13 (76,5%)	n=6 4 (23,5%)	n=0 none	n=0 none
MDS (Thrombocytopenia)	n=59 37 (62,7%)	n=59 37 (62,7%)	n=30 12 (20,3%)	n=1 none	n=1 none

■ Acute Lymphoblastic Leukemia

OP-015 Abstract Referance: 57

DETERMINATION OF THERAPEUTIC POTENTIAL OF LUTEOLIN FOR ACUTE LYMPHOBLASTIC LEUKEMIA CELLS

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Acute lymphoblastic leukemia (ALL) which is a malign hematologic cancer is characterized with increased number of lymphocytes whose developments are genetically and/or epigenetically inhibited in bone marrow. Reciprocal translocations of BCR (chromosome 22) and ABL genes (chromosome 9) lead to Philadelphia (Ph) chromosome which has tyrosine kinase activity in ALL that called as Ph+ ALL. Although tyrosine kinase inhibitors (Imatinib and Dasatinib) are used in addition to classical chemotherapy, current therapies only help to prolong lives of Ph+ ALL patients. Due to complete cure could not be succeeded novel strategies are needed for Ph+ ALL. Luteolin which has antioxidant, pro-oxidant, anti-inflammatuar and anticancer activity is a member of flavones family of flavanoids and found in many vegetables and medical herbs. According to several studies, luteolin decreases cell proliferation, tumor growth and induces apoptosis, cell cycle arrest; inhibits migration, invasion, angiogenesis and metastasis in many cancers including breast, lung, colon, prostate, gastric, chronic myeloid leukemia and acute myeloid leukemia. Bioactive sphingolipids have crucial roles in many cellular processes including proliferation, growth, apoptosis, senescence, invasion, metastasis, and drug resistance. In the literature, only one study showed that luteolin induced apoptosis through regulating sphingolipid levels in colon cancer cells.

In this study, therapeutic effects of luteolin on Ph+ ALL cells have been determined for the first time as well as the roles of bioactive sphingolipids genes on possible therapeutic potential of luteolin on Ph+ ALL cells comparing with healthy cell line. Dose and time dependent cytotoxic and cytostatic effects of luteolin were determined by MTT assay and cell cycle analysis while dose and time dependent apoptotic effect of luteolin was determined by AnnexinV-Propidium Iodide Double Staining Assay and JC-1 Mitochondrial Membrane Potential Assay through flow cytometry. Our ongoing studies will determine the effects of luteolin on expression levels of BCR/ABL and bioactive sphingolipid genes as well as human telomerase activity by both qPCR and western blotting in Ph+ ALL cells.

Therefore, the therapeutic potential a new herbal product-derived drug candidate for ALL patients with short life and low quality of life will be determined for the first time by our study.

Keywords: acute lymphoblastic leukemia, luteolin, bioactive sphingolipids

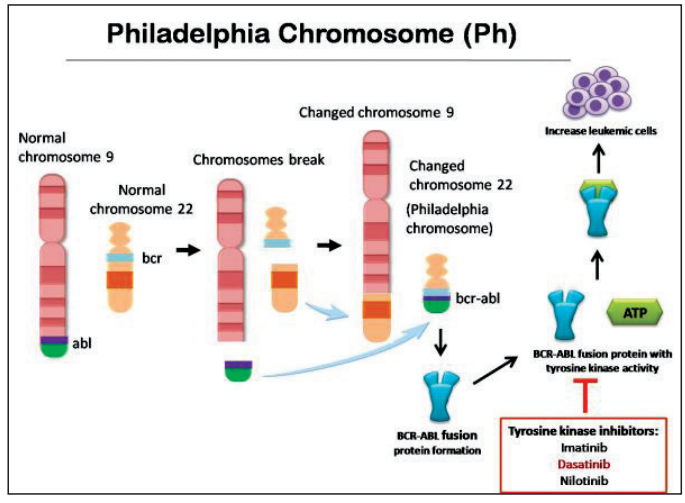

Figure 1. Philadelphia Chromosome

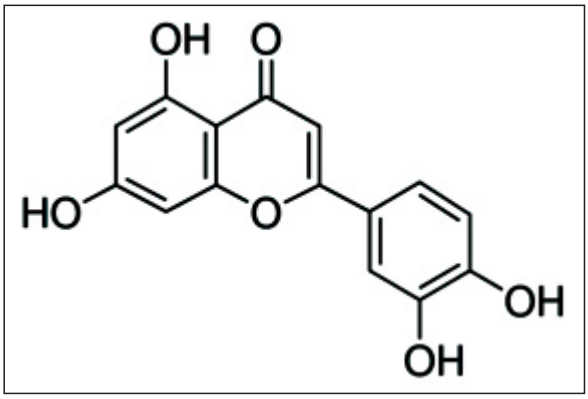

Figure 2.

■ Multiple Myeloma

OP-016 Abstract Referance: 46

MYTH OR REALITY? THE FREQUENCY AND SIGNIFICANCE OF DOUBLE HIT OR TRIPLE HIT MULTIPLE MYELOMA AT A SINGLE CENTER IN NORTHWESTERN TURKEY

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Introduciton: Risk stratification of Multiple Myeloma (MM) is based on Floresence in Situ Hybridization (FISH) method. High risk MM is defined as having at least one of the mutations related with poor prognosis including; t(4;14) t(14;16), t(14;20), del 17p, p53 mutation, gain 1q and del 1p. Mayo clinic's recent M-Smart MM risk stratification guidelines proposed a fresh point of view as having two of the high risk genetic abnormalities should be named as double hit MM and having any three as triple hit MM. From this perspective, double or triple hit MM might be related with poorer outcome. As more risk stratification tools are developed with sophisticated tools including genetical evaluation, the initial and consecutive treatment approaches for patients in these poor risk groups are not established. In this study, we aimed to evaluate the frequency and the significance double hit, triple hit myelomas in newly diagnosed patients.

Patients and Methods: Data of 163 patients diagnosed with MM between May 2014 and December 2018 at Trakya University Medical School of Faculty were evaluated retrospectively. FISH analyses for TP53/CEN17, D13S319 for 13q14, 13q34 (LSI13q34), t(4;14) (p16;q32) (LSI FGFR3/IGH Dual Color, Dual Fusion Translocation Probe Set), t(11;14) (q13;q32) (LSI CCND1/ IGH Dual Color, Dual Fusion Translocation Probe Set), t(14;16)(q32;q23) (LSI IGH/ MAF Dual Color, Dual Fusion Translocation Probe Set), CKS1B/CDKN2C (P18) Amplification/Deletion Probe (CytoCell, Cambridge, UK) were performed on bone marrow samples. A total of two hundred nuclei were enumerated for each FISH Panel probe and cut off for detection of deletion/ fusion signal in normal individuals was taken as 3%. The first line treatment agents, ISS stages, demographic and clinical characteristics and overall survival were recorded from files.

Results: Mean age at diagnosis was 64,62 ± 11,07 years. 76 patients were male and 83 were female. 24 patients were with one high risk, 7 patients with two high risk and 2 patients with three high risk determiners. 61,6% of the patients have received a triple regimen with bortezomib, cyclophosphamide, dexamethasone (CyBorD) in the first line setting. % 17,6 of the patients received bortezomib, dexamethasone and % 1,9 of the patients received bortezomib, thalidomide, dexamethasone. 47 of the 159 patients (% 29,6 of the study) proceeded with ASCT in the upfront setting. (Detailed information were given in Table 1). Overall survival of the patients with two high risk abnormality was 6 ± 4,2 months, patients with one high risk abnormality was 32,0 ± 25,6 months and patients with no high risk abnormality was 57,0 ± 9,6 months.

Discussion: Novel drugs have changed the outcome and dramatically prolonged the survival of MM risk patients. However, challenges regarding treatment of high risk MM patients still remain an unsettled issue. As double hit or triple hit lymphomas need more intensive treatment compared to standard first line treatment, it may be attributed to MM as a concern that double hit or triple hit MM patients should also be treated more intensively. In our study, patients with one or two high risk abnormalities had lower overall survival than patients with no high risk abnormality.

The evolution of MGUS to overt MM with addition of extra genetic evolution and instability step by step show us a great example of cancer stem cell theory. Double or tiriple hit MM may find their place as the last ring in this theory.

Keywords: Multiple Myelome, Double Hit, Triple Hit , FISH

Table 1. Demographic and Clinical Characteristics of the Patients

	No high risk Cytogenetic abnormality (n=126)	*One high Risk Cytogenetic Abnormality (n=24)*	*Two High Risk Cytogenetic Abnormality (n=7)*	*Three High Risk Cytogenetic Abnormality (n=2)*	*Total (n=159)*
Age (years)	64,5±11,5	65,4±9,4	61,6±9,9	71,0±4,2	64,6±11,1
Gender (male/ female)	60/66	12/12	2/5	2/0	76/83
ISS Stage at Dignosis					
Stage 1	70 (%58,8)	1 (%4,3)	0	0	71(%47,0)
Stage 2	44 (%37,0)	8 (%34,8)	1 (%14,3)	0	53(%35,1)
Stage 3	5 (%4,2)	14 (%60,9)	6 (%85,7)	2 (%100,0)	27(%17,9)
First Line Treatment					
VCD	75 (%59,5)	14(%58,3)	7 (%100,0)	2(%100,0)	98(%61,6)
VD	25 (%19,8)	3 (%12,5)	0	0	28(%17,6)
VTD-PACE	0	3 (%12,5)	0	0	3(%1,9)
Others	26 (%20,7)	4 (%16,7)	0	0	30(%18,9)
Upfront ASCT	39 (%31,0)	7 (%29,2)	1 (%14,3)	0	47(%29,6)
Overall Survival (months)	57,0 ± 9,6	32,0 ± 25,6	6 ± 4,2	-	50,0±11,0

■ Multiple Myeloma

OP-017 Abstract Referance: 68

THE COMPARISON OF THE RELATIONSHIP BETWEEN POLYNEUROPATHY FREQUENCY AND CLINICAL AND LABORATORY FINDINGS IN MULTIPLE MYELOMA CASES

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Aim: Multiple myeloma (MM) patients compose approximately 10% of patients with hematological malignancies. Polyneuropathy (PN) is one of the most important complications related to the disease and treatmentc.

Materials and Methods: A total of 121 MM cases followed in the Hematology Clinic of Atatürk Training and Research Hospital between 2010-2018 were included in the study. Electromyography results were evaluated retrospectively and clinical and laboratory findings were compared. Five cases with diabetes mellitus were excluded from the study. Chi-square method was accepted as statistically significant p <0.05.

Results: The median age of the patients was 64.5 (min 39 max: 88), and Female / Male ratio was 51/65 (44% / 65%). Demographic data of 28 (24.3%) patients with PN and 87 (75.7%) patients without PN were presented in Table 1. Renal function tests were normal in 64 (55.7%) of 87 patients without polyneuropathy (p = 0.005). There were 28 (23%) cases with extramedullary plasmacytoma larger than 1.5 cm which were detected by MR imaging at the time of diagnosis. In cases with extramedullary plasmacytoma, the prevalence of polyneuropathy was higher at the initial diagnosis (p = 0.012).

Discussion: There are publications in the literature showing that PN is associated with perineural and perivascular monoclonal immunoglobulin accumulation in MM. In our cases, there was no correlation between the presence of PN during diagnosis and the immunoglobulin subtype, but it was found to be related to the presence of renal dysfunction and the presence of extramedullary plasmacytoma. And we think that this result is the considerable.

Keywords: Multiple myeloma, Extramedullary Plasmacytoma, Polyneuropathy, Renal failure

Table 1. Comparison of the data of MM cases with and without Polyneuropathy

	Patients with Polyneuropathy n(n%): 28 (24.3%)	*Patients without Polyneuropathy n(n%): 87 (75.7%)*	*P Value*
≥ 65 years old	11 (39.3%)	48 (%55.2)	>0.05
Gender (F/M)	14/14 (50%/50%)	37/50 (42.5%/ 57.5%)	>0.05
Light chain / Heavy chain	4 (3.5%)/16 (13.9%)	24 (20.9%)/71 (61.7%)	>0.05
Immunoglobulin Subtype: IgG kappa / IgG lambda / IgA kappa / IgA lambda / Lambda light chain / Kappa light chain	11 (39.3%)/ 6 (21.4%)/ 3 (10.7%)/ 4 (14.3%)/ 4 (14.3%)/ 0 (0%)	33 (37.9%)/ 17 (19.5%)/ 15 (17.2%)/ 6 (6.9%)/ 9 (10.3%)/ 7 (8%)	
ISS: I/ II/ III	9 (32.1%)/ 6 (21.4%)/ 13 (46.4%)	25 (28.7%)/ 25 (28.7%)/ 37 (42.5%)	
Beta 2 microglobulin ≥3.5 mg/L	14 (50%)	34 (39.1%)	>0.05
Albumin ≤3.5 g/dL	12 (42.9%)	32 (36.8%)	>0.05
Hemoglobin ≤10 g/dL	20(71.4%)	51 (58.6%)	>0.05
Calcium ≥12 mg/dL	6 (21.4%)	16 (18.4%)	>0.05
Creatinine ≥2 g/dL	16 (57.1%)	23 (26.4%)	0.005
Extramedullary plasmacytomas	12 (42.9%)	16 (18.4%)	0.012
Lytic bone lesions	18 (64.3%)	52 (59.8%)	>0.05
Pathologic fracture	9 (32.1%)	24 (27.6%)	>0.05

■ Multiple Myeloma

OP-018 Abstract Referance: 149

PRE-TRANSPLANT HEMOGLOBIN AND SERUM CREATININE LEVELS CORRELATE WITH PROGRESSION FREE SURVIVAL IN MYELOMA PATIENTS UNDERGOING AUTOLOGOUS STEM CELL TRANSPLANTATION

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Ankara University School of Medicine, Department of Medicine

Background: High dose melphalan and autologous stem cell transplantation (ASCT) significantly prolong survival for patients with multiple myeloma (MM). However, prognostic biomarkers in ASCT are needed to improve risk assessment and help guide therapeutic and surveillance strategies to alleviate the risk of death from the procedure. The purpose of this study is to assess the effects of hemoglobin (Hgb) and serum creatinine (Crea) values at the time of transplantation on the overall outcome of patients with multiple myeloma treated at our transplant center.

Material & Methods: This analysis included 247 consecutive patients who underwent ASCT for MM between 2010-2016. Hemoglobin was grouped as low or high relative to their sample median. Patients were also stratified according to serum Crea value at the time of transplantation (<2 or ≥2 mg/dl).

Results: The median age was 57 (29-75) years and most patients were male (n=151, 61.1%), IgG subtype (n=124, 50.2%), and ISS stage 3 (n=122, 49.4%). The interval from the time of diagnosis to ASCT was median 7 months and median follow-up from ASCT was 49 months (range, 3-198 months). The most commonly induction regimens included VAD (vincristine, doxorubicin and dexamethasone) and VCD (bortezomib, cyclophosphamide, dexamethasone), respectively. Since maintenance was not an approved treatment in myeloma most patients did not receive any. For the entire cohort, the median Hgb and Crea were 11.5 g/dL and 0.9 mg/dL respectively. No difference in progression free survival (PFS) was observed between a lower and higher Hgb (82 vs. 81 months, p=0.96). However, the median PFS was significantly longer in patients with a lower Crea compared to those with a higher Crea (83 vs. 48 months, p=0.01). Patients with both a lower hemoglobin and higher Crea experienced shorter PFS compared to those with a higher hemoglobin and lower Crea (45 vs. 82 months, p<0.001). We failed to demonstrate the impact of creatinin levels on time to neutrophil and platelet engraftment. There were no differences in OS according to lower vs. higher Hgb (58 vs. 52 months; p=0.29, respectively) but in higher crea cohort worse OS was observed (41 months vs. 57 months; p=0.02, respectively).

Conclusions: We demonstrate that hemoglobin and creatinine represent important determinants of clinical outcomes after ASCT. A lower hemoglobin and higher creatinine, individually and when combined, were associated with shorter PFS. Therefore, further studies of larger randomized cohorts are required to clarify the impact of pre-transplant Hgb and Crea levels on ASCT outcomes.

Keywords: Multiple myeloma, Autologous Stem Cell Transplantation, Hemoglobin, Serum Creatinine

■ Other

OP-019 Abstract Referance: 50

THE CORRELATION BETWEEN INTERIM IMAGING RESULTS AND DISEASE PROGNOSIS OF PATİENTS WİTH HODGKIN AND DIFFUSE LARGE B CELL LYMPHOMA: SINGLE CENTER EXPERIENCE

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Objective: In our study, we aimed to investigate the relationship between the interim imaging response and disease prognosis in patients with Hodgkin (HL) and Diffuse Large B-Cell Lymphoma (DLBCL).

Materials and Methods: The study included 90 DLBCL and 67 HL patients observed in Dokuz Eylul University (DEU) Hospital Department of Hematology. The pre-treatment and interim PET / CT (I-PET/CT) images of 121 patients who underwent imaging with PET/CT were evaluated by two nuclear medicine physicians as a blind experiment. The first and interim CT (I-CT) images of 53 patients who underwent imaging with contrast-enhanced CT were evaluated by a two radiology physicians as a blind experiment. Patients' interim responses and end-treatment responses were compared using the SPSS 22.0 statistical analysis program.

Results: According to I-PET / CT positivity or negativity and post-treatment disease status; the positive (PPV) and negative predictive value (NPV) of the method were calculated separately for both HL and DLBCL patient groups. I-PET / CT PPV was 36% for HL, 61.9% for DLBCL; NPV was 95.4% for HL and 93.1% for DLBCL. The 7-year progression-free survival rate was 54% for I-PET / CT + patients and 83% for I-PET / CT - patients in HL; DLBCL was also 20% for

I-PET / CT + patients and 79% for I-PET / CT - patients. I-CT response was negative despite I-PET / CT positivity for 2 of 8 patients who were evaluated with both of PET / CT and contrast-enhanced CT in the DBBHL group. I-CT response was positive despite I-PET / CT negativity for 3 of 9 patients who were evaluated with both of PET / CT and contrast-enhanced CT in the HL group. In a group of 157 patients, when assessed based on the kappa analysis it was found that there was no agreement between Lugano I-PET / CT related response and Lugano and RECIST 1.1 I-CT related responses. On the other hand, a higher agreement was determined between the end-of-treatment response and the I-PET / CT-related response group compared to the I-CT groups.

Conclusion: PET / CT scans significantly improved the assesment of treatment responses. Compared with CT, PET/CT prevented some early-stage patients' being treated with unnecessary intensive therapies and some advance stage patients' being treated with less intensive therapies. I-PET/CT negativity has a high prognostic value in terms of progression-free survival, and this may be helpful for clinicians to reduce the number of cures and the intensity of treatment. Treatment intensification based only on I-PET/CT positivity may cause patients to be exposed to unnecessary drug toxicity.

Keywords: lymphoma, interim assesment, PET/CT

■ Chronic Lymphocytic Leukemia

OP-020 Abstract Referance: 66

WHICH MARKERS SHOULD BE USED FOR CHRONIC LYMPHOCYTIC LEUKEMIA SCORING SYSTEM BY IMMUNOPHENOTYPING ?

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CLL is one of the most common diagnoses made by flow cytometry laboratories. As there is no pathognomic molecular anomaly in CLL, flow cytometry is almost the gold standard for diagnosis. The scoring system used for diagnosing CLL has some limitations. Not every laboratory can consistently and reproducibly determine weak expressions of sIg, CD22/CD79b. In the present study we assessed the importance of the expressions of CD43, CD81, CD20, and ROR1, which are not present in the scoring system for CLL, for the differential diagnosis of CLL, and their expressions in non-CLL cases

Methods: We performed immunophenotyping from peripheral blood or bone marrowaspiration samples of 165 cases using 8 color flow cytometry. We retrospectively evaluatedall cases' diagnoses, immunophenotypic features, and morphological, histopathological, andmolecular data.

Results: CD43 positivity was sensitive but of lower specificity. It had a high diagnostic power (sensitivity 100% , specificity 88.5% AUC 98.0%)CD200 was a sensitive marker for CLL (sensitivity 98% and specificity 90%, AUC: 96%) CD81 negativity for CLL had a sensitivity of 95%, specificity of 82% , and AUC of 92%. ROR1 was positive in all CLL and MCL cases. CD79b was a highly specific and sensitivemarker for MCL.

Discussion: CD43, CD81, CD200, and ROR1 should be definitely inlcuded in diagnostoc algorithms for the differential diagnosis of CLL especially from MCL.

Keywords: CD43,CD81, CD200, ROR1; chronic lymphocytic leukemia; B-cell lymphoproliferative disorder

Table 1.

CD name	*AUC%*	*Sensitivity%*	*Specifity%*
CD43	98	100	88
CD81	92	95	82
ROR1	95	94	90
CD200	96	98	90
CD22	90	92	80
CD23	97	99	92
CD79b	77	70	95
sIg	50	51	64

■ Other

OP-021 Abstract Referance: 159

MERSIN UNIVERSITY LAST DECADE EXPERIENCE WITH MYELOFIBROSIS

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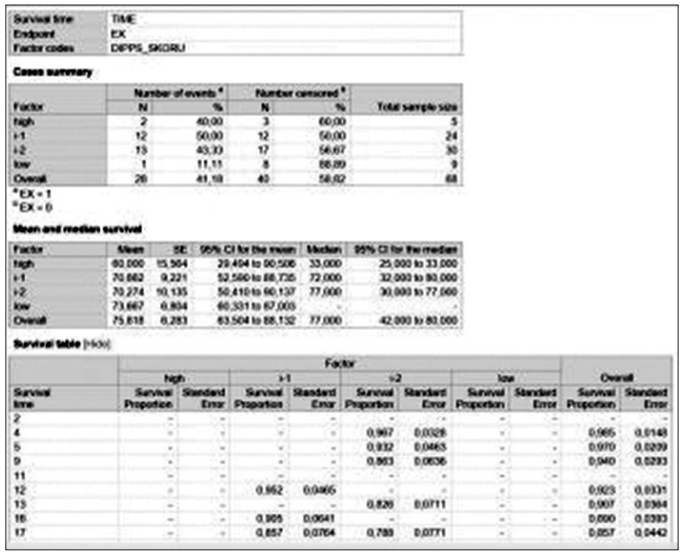
Objective: To document the Mersin University last decade experience with primary myelofibrosis and provide mature risk-stratified survival data and disease complication estimates

Patients and Methods: Mersin University patients with World Health Organization–defined primary myelofibrosis diagnosed between 2009-2019 constituted the core study group. Clinical and laboratory data were abstracted from medical records. Risk-stratification used conventional risk models considering age, leukocytes, and thrombosis, dynamic international prognostic scoring system. Statistical analyses were based on parameters obtained at the time of referral to MU which, in the majority of cases, coincided with or was within 1 month of diagnosis. All patients were followed from diagnosis until death or date of last follow-up/contact. .

Results: A total of 74 patients (median age, 60,5 years; range, 30-85 years) were considered; 3 PV, 5 ET, 1 CML and 8 MDS 57 PMF. Number of males 35(47,3%) and females 39 (52,7%) From October , 2009, through , October 2019, 34 deaths (45,9%), 3 leukemic transformations (4%), and 3 thrombotic events (4,2%) were recorded. Median overall survival (OS) was 6 years. PMF cases were attributed low (12,2%), intermediate-1 (32,4%) -2 (40,5%) and high (6,8%) risk. Documented median hemoglobin levels were 9,75 g/dL (range, 3.8-20 g/dL). Furthermore, 20 of 74 evaluable patients (27%) overall were transfusion dependent. Platelet counts were 510109 /L (range, 4-2228000 /L). Median leukocyte counts were 9.140 /L (range, 1420-290000 /L) . the median peripheral blood blast percentage was 2% (range, 0%- 10%; 17%). 30 of 74 evaluable patients abnormal karyotype was documented 4,1%. Constitutional symptoms and palpable splenomegaly were documented in 23% (n=17) and 92% (n=47) of 74 and 51 evaluable patients. A history of hemorrhage at or before diagnosis was present in 3 patient 4,2%. Overall, 2 patients (2%) with PMF underwent allogeneic stem cell transplant.

Conclusion: This study provides mature survival and outcomes data in myelofibrosis. One of the results is statistically that the life curves do not differ significantly or the factor (underlying disease type) has no significant effect on the survival time.(chi square statistic 1,9945 and p:0,7368 >0,05). In the literature Survival was significantly different among the 4 risk categories ($P < .001$).(1) median survival was 14.6 years in low-risk patients, 7.4 years in intermediate-1, 4 years in intermediate-2, and 2.3 years in high risk. In our study Dipps Scores has no effect until the time to exitus.(chi square value 3,1392 and p:0,3707 >0,05).and median survival was 72 months in intermediate-1, 77 months in intermediate-2, and 33 months in high risk. Comparison of Ruxolitinib and the other medications has no prominent difference on life expectancy. .(chi square value 3,5149 and p:0,0608 >0,05). Hereby miyelofibrosis is a serious disease with high mortality and there is need for effective disease treating agents

Keywords: myelofibrosis



Survival time	TIME
Endpoint	EX
Factor codes	DIPPS_SKORU

Cases summary

Factor	Number of events * N	Number of events * %	Number censored * N	Number censored * %	Total sample size
high	2	40,00	3	60,00	5
i-1	12	50,00	12	50,00	24
i-2	13	43,33	17	56,67	30
low	1	11,11	8	88,89	9
Overall	28	41,18	40	58,82	68

* EX = 1
* EX = 0

Mean and median survival

Factor	Mean	SE	95% CI for the mean	Median	95% CI for the median
high	60,000	15,564	29,494 to 90,506	33,000	25,000 to 33,000
i-1	70,662	9,221	52,590 to 88,735	72,000	32,000 to 80,000
i-2	70,274	10,135	50,410 to 90,137	77,000	30,000 to 77,000
low	73,667	6,804	60,331 to 87,003	-	-
Overall	75,818	6,283	63,504 to 88,132	77,000	42,000 to 80,000

Survival table [Hide]

	Factor									
	high		i-1		i-2		low		Overall	
Survival time	Survival Proportion	Standard Error	Survival Proportion	Standard Error	Survival Proportion	Standard Error	Survival Proportion	Standard Error	Survival Proportion	Standard Error
2	-	-	-	-	-	-	-	-	-	-
4	-	-	-	-	0,967	0,0328	-	-	0,985	0,0148
5	-	-	-	-	0,932	0,0463	-	-	0,970	0,0209
9	-	-	-	-	0,863	0,0636	-	-	0,940	0,0293
11	-	-	-	-	-	-	-	-	-	-
12	-	-	0,952	0,0465	-	-	-	-	0,923	0,0331
13	-	-	-	-	0,826	0,0711	-	-	0,907	0,0364
16	-	-	0,905	0,0641	-	-	-	-	0,880	0,0393
17	-	-	0,857	0,0764	0,788	0,0771	-	-	0,857	0,0442

Figure 1. Passamonti F, Cervantes F, Vannucchi AM, et al. Blood. 2010;115:1703-1708.

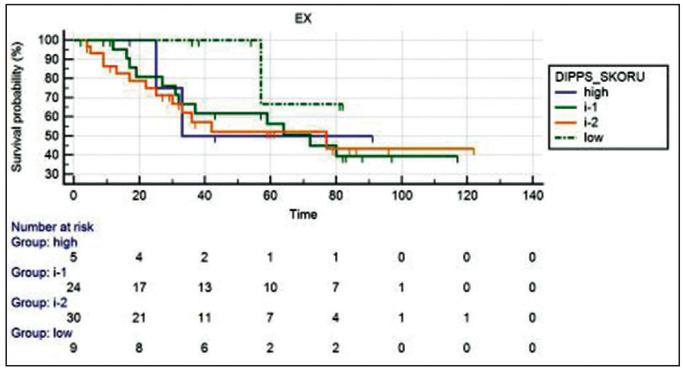


Figure 2.

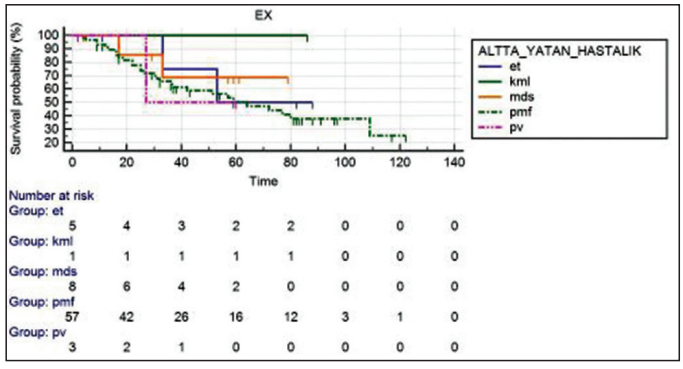


Figure 3.

■ Multiple Myeloma

OP-022 Abstract Referance: 138

RETROSPECTIVE EVALUATION OF IMMUNOMUDULATORY AGENTS RESPONSE AND SIDE EFFECTS IN RELAPSED REFRACTOY MYELOMA PATIENTS: REAL LIFE EXPERIENCE

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Objective: Multiple Myeloma is a clonal plasma cell disease leading to renal failure, hypercalcemia, anemia and destructive bone lesions. The overall survival (OS) has significantly improved with the usage of immunomodulatory drugs (IMIDs) and proteosome inhibitors. But there are various side effects that can affect the effective usage of these drugs. In this study, we aimed to review management of side effects of IMIDs in our daily practice and reveal their treatment responses.

Method and Results: Demographic data, survival and response conditions of eighty-five patients who were treated with IMIDs in Dokuz Eylul University between 2001-2018 were evaluated retrospectively.

Results: Median age was 62 (38-83). Median follow-up time was 57 months (5-177). At the end of follow-up time, 34.7% of the patients were dead. Median overall survival was 77 months (61.4-92.6). IMIDs were used in relapsed/refractory myeloma for all patients. After the first line treatment, very good partial remission (VGPR) was obtained in the 87.1% of the patients. Others had stabil diseases. Autologous transplantation was made in the 57.6% of the patients. IMIDs usage at relapsed disease was as follows: 12.9% thalidomide (27.2% 2. line,36.4% 3.line, 36.4% other), 91.8% lenalidomide (12.8% 2.line, 82.1% 3.line, 5.1% other), 17.6% pomalidomide (all after 3.line). Pomalidomide had used after lenalidomide generally. The most common side effect during thalidomide was neuropathy (63.6% grade 2-3 neuropathy). VTE was not observed. VTE prophylaxis like acetylsalicylic acid had been used 54.5% of the patients during thalidomide therapy. None of the patients left thalidomide due to side effects. Median lenalidomide use was 12 months (1-46). Response rates were as follows: 39.7%PR, 34.6%VGPR, 14.1% CR. 62.8% of the patients had received antibiotic prophylaxis. All patients had been taken VTE prophylaxis (75.7% ASA, 24.3% ASA+ LMWH). Grade 1-2 neutropenia was seen at the 69.2% of the patients, grade 1-2 thrombocytopenia was 33.3%, grade 2 anemia was 10.3%. G-CSF was used in 23.1% of the patients. DVT was found in 5.1% of the patients, pulmonary thrombosis was found in 5.1% of the patients in prophylaxis group. The most common side effect was infection (mostly pneumonia). Hepatotoxycity rate was 7.7%. Lenalidomide was interrupted at 32.1% of the patients mostly due to infection for median 7 days. Infection rate was 14.2% at the antibiotic prophylaxis group while 58.8% at other group. During pomalidomide therapy, antibiotic prophylaxis were given for 73.3% of the patients, DVT prophylaxis were given for all patients. Neutropenia was seen as 73.3% of the patients. Infection rate was 73.3%. 2/11 patients died due to sepsis. These patients were refractory for all anti-myeloma therapy also.

Conclusion: IMIDs are frequently used at relapsed/refractory setting in Turkey. Infections, DVT can cause drug interruptions or dose reductions in some cases. These may affect the effectiveness of therapy. To be able to use these drugs effectively, we should take care to use prophylactic approaches.

Keywords: Keywords: IMIDs, immunomudulatory drugs, side effects, multiple myeloma

■ Multiple Myeloma

OP-023 Abstract Referance: 150

CAN AUTOLOGOUS STEM CELL TRANSPLANTATION ABROGATE THE POOR PROGNOSIS ASSOCIATED WITH HIGH LDH?

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Background: Multiple myeloma (MM) is a plasma cell neoplasia characterized by a diffuse clonal plasma cell infiltration of the bone marrow. Serum lactate dehydrogenase (LDH) is a relevant biomarker in MM and in the era of novel agents, LDH confirmed its negative impact on survival in newly diagnosed setting (Bal et al., presented at ASH2018).

Methods: This single center retrospective study included 208 patients with a diagnosis of MM who underwent ASCT at our center between January 2008 - Mart 2018 were prospectively analyzed. We identified patients with baseline serum LDH values (ULN=247 U/L). We compare baseline characteristics and outcomes of ASCT according to LDH values.

Results: All clinical data were available in 208 cases (High LDH: 92 (44.2%), Normal LDH: 116 (55.8%)). There were 87 (41.8 %) female and 87 (41.8 %) male patients. The median age at diagnosis of MM was 63 years (range, 37-77 years). The median time of follow-up was 48 months (range, 2.8-197.5 months). Of the 92 patients with high LDH who underwent ASCT, median age was 65 years and ECOG performans status was 1 and 58.6 % were male. Induction therapy consisted of ≥ 3 drugs in 5.4 % and 2 drugs in 35.9 %. Forty-eight (53.3%) patients with high LDH received a bortezomib-based induction and 35 patients (40.2 %) achieved ≥ very good partial remission (VGPR) after the induction therapy. During follow up, 45 relapses were occurred and all relapsed patients died. According to the long-rank test, estimated 5-year OS was not significantly different between normal and high LDH categories (63.3 %±0.6 % vs. 64.6 %±0.5 %; p=0.99) (Figure-1). Median PFS was 101.4 months (95% CI: 73.7-129) in high LDH group and 92.1 months (95% CI: 71.1-113.1) in normal LDH group (p=0.99).

Conclusion: Elevated LDH was confirmed as a poor prognostic factor in previous reports. In our transplanted patients with high LDH cohort, clinical outcomes are favorable and similar those have normal LDH. Therefore, further studies of larger randomized cohorts are required to clarify the impact of pre-transplant LDH levels on ASCT outcomes.

Keywords: Multiple myeloma, Serum lactate dehydrogenase Autologous Stem Cell Transplantation

■ Stem Cell Transplantation

OP-024 Abstract Referance: 90

COLLECTION OF STEM CELLS ≥ 5.0 X 106/Of BODY WEIGHT IN ONE DAY IN MULTIPLE MYELOMA IN THE PROCESS of AUTOLOGOUS STEM CELL TRANSPLANTATION

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Introduction: Autologous hematopoietic stem cell transplantation (ASCT) is an established treatment for patients with hematologic malignancies. Requested $CD34^+$ cell dose needed to ensure hematopoietic recovery following ASCT is 2.5 cells $x10^6$/of body weight, and 5.0 cells $x10^6$/of body weight (BW) for two ASCT in patients with multiple myeloma.

The aim of study was to analyse absolute number of cells (ANC) CD34+ ≥40.01 $x10^6$ /L in peripheral blood as guarantor of successful apheresis for two ASCT in patients with multiple myeloma (MM).

Patients and methods: The study was conducted in a retrospective-prospective manner. In the Clinic of Hematology, Clinical Center University of Sarajevo, during period April 2013-March 2019, treatment with high-dose therapy and ASCT was performed 94 patients who underwent 145 apheresis: 33pts (35%) with MM; 22pts (23%) with Hodgkin lymphoma; and 39pts (42%) with non-Hodgkin lymphoma. Collection performed in one day were characterized by the number collected CD34+ cells into two groups: collection of CD34+ cells <5.0 $x10^6$/BW; and ≥5.00 $x10^6$/BW. We examined correlation of CD34+ cells collection according to ANC CD34+ in peripheral blood by apheresis per day. Independent analyzed variables were: CD34+ cell dose, age, gender, disease.

Results: The average age of patients was 45 years, youngest was 18 and the oldest was 68 years. The group consisted of 17 males (51,52%) and 16 (48,48%) female patients. Collection of CD34+ < 5.0 $x10^6$/BW occurred in 27 (62,79%) cases; while collection of CD34+≥ 5.0 $x10^6$/BW was achieved in 16pts (37.21%). All the patients that achieved collection of CD34+ ≥ 5.0$x10^6$/BW in one day had 100% ANC CD34+ ≥40.01 $x10^6$/L in peripheral. Displayed difference was statistically significant p=0.0001. For statistical analysis, we used the c^2 test, Kolmogorov Smirnov and Mann-Whitney U test. P<0.05 was considered significant.

In conclusion: the guarantor of collection≥5.0 cells $x10^6$/BW is ANC CD34+ ≥40.01 x 10^6/L in peripheral blood on the day of apheresis.

Keywords: Myeloma multiplex, ANC in peripheral blood, collection