

Research No. (1): Single Author

Pretreatment Factors Predicting Sustained Virological Response to Pegylated Interferon/Ribavirin Combination Therapy in Egyptian Patients with Hepatitis C Virus Genotype 4

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Abstract:

Background: Hepatitis C virus (HCV) is a growing health problem worldwide. Egypt has the highest HCV prevalence in the world. In the last decade, HCV-related morbidity doubled, and HCC related to HCV increased almost threefold. The desired goal with combination antiviral therapy is to obtain a sustained virologic response (SVR). The predictors of SVR of genotype-4 are not well represented because most of the data were on genotype-1; therefore, there is a need for further studies.

Aim: To clarify the predictors of SVR to combination therapy in patients with HCV infection genotype-4 before initiating treatment. Patients and Methods: This retrospective study included 530 HCV patients treated with combination therapy pegylated interferon plus ribavirin. The patients were divided into two groups: SVR patients (Group I) and Non-SVR patients (Group II).

Results: A significantly higher age was found in group II when compared with group I (P=0.0008). Also, a significantly higher pretreatment ALT, AST, alkaline phosphatase and HCV-RNA viral load levels were found in group II when compared with group I (P< 0.0001) for all. Patients with (age >40 years, pretreatment ALT level >2 folds, bilharziasis history, late fibrosis stages and late activity stages) were prone to be non-SVR than the others.

Conclusion: Patients with (age >40 years, pretreatment ALT level >2 folds, bilharziasis history, late fibrosis stages and late activity stages) were prone to be non-SVR than the others. These findings may have important prognostic, cost saving and therapeutic implications in HCV patients treatment.

Key words: Predictors of SVR, hepatitis C virus, pegylated interferon, ribavirin

Research No. (2): Multiple Authors

Serum Resistin and Insulin Resistance as Risk Factors for Hepatocellular Carcinoma in Cirrhotic Patients with Type 2 Diabetes Mellitus

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Life Sci J 2014; 11(11):941-949

Abstract:

Background: Hepatocellular carcinoma (HCC) is the sixth most common cancer and the third leading cause of cancer related death. At least 25% of HCC cases do not have any known etiology. Approximately 2-fold higher risk of HCC in diabetic patients. The causal nature of this positive association involves complex mechanisms that have not yet been conclusively described. Previous studies have suggested that elevated levels of insulin and insulin growth factor (IGF) may play important roles in HCC. Resistin is a polypeptide hormone belonging to adipokines and could contribute to tumorigenesis and angiogenesis

Aim: to study serum resistin and insulin resistance as risk factors for HCC in hepatitis C virus (HCV) cirrhotic patients with type 2 diabetes mellitus.

Subjects and Methods: 50 adult patients with HCV infection were selected for this study. They were categorized into: (Group I) which included 25 type 2 diabetes mellitus (DM) patients with cirrhosis and HCC and (Group II) which included 25 type 2 DM patients with cirrhosis only. 25 healthy subjects, age and sex-matched, were enrolled as controls (Group III). Routine tests for DM, HCV, liver cirrhosis & HCC were done. HOMA-IR and serum resistin were assessed in all groups.

Results: HCC diabetic patients (Group I) showed significantly higher mean values of HOMA-IR and resistin than cirrhotic diabetic patients (Group II) and the control subjects (Group III). Frequency of low value for HOMA-IR index (>2.5) was not significantly different between HCC (Group I) and cirrhotic (Group II) patients but Frequency of high value for HOMA-IR index (>4) was significantly different between HCC and cirrhotic patients with higher frequency in HCC patients (Group I) (76%) when compared with cirrhotic patients (Group II) (4%). In HCC patients (Group I), significant positive correlations were found between HOMA-IR and both fasting insulin and α - Fetoprotein (AFP). Significant positive correlations were found between resistin, and both fasting insulin and AFP. Positive correlation was found between HOMA-IR & resistin in (Group I) & (Group II).

Conclusions: HOMA-IR and serum resistin measurement could represent novel markers to identify the HCV cirrhotic patients with type 2 DM at greater risk for the development of HCC. These findings may have important prognostic and therapeutic implications as insulin resistance (IR) is a potentially modifiable factor.

Key words: Hepatocellular Carcinoma, Hepatitis C virus, Insulin resistance, Resistin, Type 2 Diabetes Mellitus

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Research No. (3): Single Author

Prevalence and chemotherapy-induced reactivation of occult hepatitis B virus among hepatitis B surface antigen negative patients with diffuse large B-cell lymphoma: Significance of hepatitis B core antibodies screening

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Abstract:

Background: Occult hepatitis B infection (OBI) is characterized by negative hepatitis B surface antigen (HBsAg) and detectable hepatitis B virus (HBV)-DNA in the liver and/or serum, with or without hepatitis B core antibody (anti-HBc). Anti-HBc is the most sensitive marker of previous HBV. HBV reactivation in patients under immunosuppressive treatment is life-threatening, occurring in both overt and occult HBV especially in hematological malignancies.

Aim of the work: To evaluate the prevalence and chemotherapy-induced reactivation of OBI among hepatitis B surface antigen negative patients with diffuse large B-cell lymphoma (DLBCL) patients and to determine the significance of anti-HBc screening among this group of patients before receiving chemotherapy.

Patients and methods: This cross-sectional study included 72 DLBCL patients negative for HBsAg, HBsAb and hepatitis C virus antibodies (anti-HCV). Patients were subjected to investigations including anti-HBc. All patients underwent alanine transaminase (ALT) monitoring before each cycle of chemotherapy and monthly for 12 months after the end of chemotherapy. Patients with suspected OBI were tested for HBV-DNA using real-time polymerase chain reaction (PCR).

Results: Anti-HBc was detected in 10 of 72 HBsAg negative sera (13.89%) (95% confidence interval 6.9–22.2%). Five of the 10 anti-HBc positive patients in this study had OBI reactivation.

Conclusion: The study concluded that anti-HBc screening is mandatory before chemotherapy. HBsAg-negative/anti-HBc-positive patients should be closely observed for signs of HBV reactivation through the regular monitoring of ALT. Prophylaxis lamivudine is recommended for anti-HBc positive patients before chemotherapy.

Keywords: Hepatitis B virus; HBsAg; HBV-DNA; Anti-HBc; Occult HBV reactivation; Diffuse large B-cell lymphoma

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Research No. (4): Multiple Authors

Plasma Levels of CXCL 9, 10, 11 and 12 and Their Impact on Overall Survival in Chronic Lymphocytic Leukemia

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Life Sci J 2015; 12(4):24- 32

Abstract:

Background/Aims: Background/Aims: The expression of chemokines is altered in chronic lymphocytic leukemia (CLL) due to inactivation of the tumor suppressor genes or constitutive activation of the oncogenes. The aim of this study was to measure plasma levels of chemokines CXCL9, 10, 11 and 12 in CLL and relate that, if any, with abnormal immunophenotype considered with bad prognosis.

Methods: Plasma from 40 CLL patients and 20 healthy age and gender-matched controls were analyzed for CXCL 9, 10, 11 and 12 by enzyme-linked immunosorbent assay.

Results: CXCL11 and 12 plasma concentrations were significantly higher in CLL patients compared to controls ($P=0.013$ and 0.0015) respectively. CLL patients with higher CXCL11 or 12 levels (median >128.4 , 1006.65 pg/mL respectively) before treatment had worse prognosis for overall survival (OS) ($P = 0.0342$, 0.0229).

Conclusion: High plasma levels of CXCL11 and 12, is associated with high grade CLL leukemia and may be useful as a predictive indicator for OS.

Key words: Chronic lymphocytic leukemia, CXCL 9, 10, 11, 12, survival

Research No. (5): Multiple Authors

Serum cystatin-C and urinary *N*-acetyl- β -D-glucosaminidase as biomarkers for early renal dysfunction in adult Egyptian patients with β -thalassemia major

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Tanta Medical Journal 2015, 43(1):31–38

Abstract:

Background/aims: β -Thalassemia syndromes are the most common inherited hemoglobinopathies. In Egypt, 1000/1.5 million/year live borns suffered from thalassemia. β -Thalassemia major (β -TM) is the most severe form. Advances in the care of patients with β -TM, have allowed previously unrecognized complications to emerge, including several renal abnormalities. Therefore, the aim of the present study is to investigate the presence of glomerular and/or tubular dysfunctions in adults with β -TM, using biomarkers of glomerular and tubular dysfunctions.

Subjects and methods: Forty patients with β -TM (group I) were selected with 20 age-matched and sex-matched healthy participants as a control (group II). Patients were subjected to full medical history taking and complete clinical examination. Serum cystatin-C and urinary *N*-acetyl- β -D-glucosaminidase (UNAG) levels were measured.

Results: Significantly higher levels of serum cystatin-C and UNAG in thalassemic patients were observed when compared with the control group. Significantly higher levels were observed for serum cystatin-C and UNAG in patients with renal affection, poorly chelated and inadequately transfused patients. A significant positive correlation between serum cystatin-C and serum ferritin was observed and significantly negative correlations between serum cystatin-C on one hand and pretransfusional hemoglobin and estimated glomerular filtration rate on the other hand were observed. A significantly positive correlation between UNAG and the urinary albumin creatinine ratio (ACR) and significantly negative correlations between UNAG on one hand and pretransfusional hemoglobin and estimated glomerular filtration rate on the other hand were observed.

Conclusion: β -TM patients had glomerular and tubular dysfunctions. Serum cystatin-C and UNAG are promising biomarkers for monitoring glomerular and tubular dysfunction. **Keywords:** β -thalassemia major, renal dysfunction, serum cystatin-C, urinary *N*-acetyl- β -D-glucosaminidase

Keywords: β -thalassemia major, renal dysfunction, serum cystatin-C, urinary *N*-acetyl- β -D glucosaminidase

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Research No. (6): Multiple Authors

Serum thrombopoietin and platelet antibodies in thrombocytopenic patients with chronic hepatitis C virus: clinical application of platelet indices

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Egyptian Journal of Haematology 2016, 41:15–22

Abstract:

Background: Chronic hepatitis C virus (HCV) infection is prevalent in 160 million individuals worldwide. Egypt has the highest prevalence of HCV in the world. HCV is known to cause thrombocytopenia even in the absence of overt hepatic disease. The pathophysiology of thrombocytopenia with chronic HCV is complex.

Aims: To evaluate serum thrombopoietin (TPO) and platelet antibodies in thrombocytopenic patients with chronic HCV and to assess the diagnostic utility of mean platelet volume (MPV) and platelet distribution width (PDW).

Patients and methods: The present study included 70 patients with chronic HCV with thrombocytopenia divided into two groups; 20 age-matched and sex-matched HCV patients without thrombocytopenia were also included as controls. Serum TPO, platelet autoantibodies, MPV, and PDW were measured in all participants.

Results: A significantly lower serum TPO level and platelet count were found with advancing degree of liver fibrosis and activity. Significantly higher MPV and PDW were found in patients with antiplatelet autoantibodies formation. The platelet count showed significant positive correlations with TPO level, MPV, and PDW, and inverse correlations with aspartate aminotransferase, alanine aminotransferase, and viral load.

Conclusion: The dominant mechanism in mild thrombocytopenic HCV patients was the formation of antiplatelet autoantibodies, whereas in moderate to severe thrombocytopenic patients, the dominant mechanism was combined bone marrow affection and formation of antiplatelet autoantibodies. Serum TPO level was decreased in patients with HCV-induced thrombocytopenia. MPV and MPV and PDW may be used as indicators for the dominant mechanism.

Keywords: hepatitis C virus, platelet antibodies, platelet indices, thrombocytopenia, thrombopoietin

Research No. (7): Multiple Authors

Effect of Iron Deficiency Anemia on Glycated Hemoglobin and Glycated Albumin Levels in Non-Diabetic Patients: Role of Malondialdehyde

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Life Sci J 2016; 13(4):31-38

Abstract:

Background/aim: HemoglobinA1c (HbA1c) is used to assess the long-term glycemic control. Glycated albumin (GA) is a short-term glycemic marker, not influenced by hemoglobin disorders. The studies about the effect and mechanism of iron deficiency anemia (IDA) on HbA1c are conflicting and not yet known. IDA promotes oxidative stress. Malondialdehyde (MDA) found to be elevated in oxidative stress. The aim of our work to investigate the effect of IDA before and after treatment on HbA1c and GA levels in non-diabetic patients and the role of MDA in this effect.

Subjects and methods: Prospective study was conducted with 105 participants divided into two groups. Group I comprised 85 IDA patients treated with intravenous iron, 60 patients respond to treatment which complete the study. Group II included 20 apparently healthy participants as control group. Complete blood count, iron profile, HbA1c, GA and MDA were measured before treatment and after 12 weeks from the beginning of intravenous iron infusion.

Results: HbA1c and MDA are significantly higher in IDA before treatment than the controls. HbA1c and MDA decreased significantly by iron therapy. Insignificant difference between the controls, IDA patients as regard GA. Significant negative correlations between HbA1c and hemoglobin, mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), serum ferritin, serum iron and transferrin saturation. Significant positive correlations between HbA1c and total iron binding capacity (TIBC) and serum MDA.

Conclusions: GA rather HbA1c is better glycemic marker in IDA. Caution should be used when diagnosing diabetes among IDA patients using HbA1c. MDA may play a role in HbA1c elevation in IDA.

Keywords: Iron deficiency anemia; Hemoglobin A1c; Glycated albumin; Malondialdehyde

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Research No. (8): Single Author

The Utility and Applicability of Chronic Myeloid Leukemia Scoring Systems for Predicting the Prognosis of Egyptian Patients on Imatinib: Retrospective Study

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J Leuk 4: 210. doi:10.4172/2329-6917.1000210

Abstract:

Background: Chronic myeloid leukemia (CML) is myeloproliferative clonal neoplasm. Imatinib has greatly improved CML prognosis. Many prognostic scoring systems have been developed for CML risk stratification. In clinical practice, 3 systems are widely used: Sokal, Hasford and European Treatment Outcome Study (EUTOS). Recently, EUTOS long-term survival (ELTS) score is the first long-term scoring system that considered specifically CML-related death. Therefore, the aim of the present study was to validate the effectiveness of Sokal, Hasford, EUTOS and ELTS scoring systems in predicting the outcome in Egyptian CML-chronic phase (CML-CP) patients treated with imatinib.

Patients and methods: Retrospective study performed on 167 patients with CML-CP who were treated with imatinib. Using the Sokal, Hasford, EUTOS and ELTS scores, we divided the patients into each risk groups.

Results: Significant differences in event free survival (EFS), time without progression (TWP) and overall survival (OS) prediction between the Sokal, Hasford and ELTS risk groups, but no significant difference among the EUTOS score risk groups.

Conclusion: Our study indicates that Sokal, Hasford and ELTS scoring systems but not the EUTOS score are effective in predicting early treatment response, EFS, TWP and OS for Egyptian CML patients treated with imatinib.

Keywords: Chronic myeloid leukemia; Prognosis; Sokal; Hasford; EUTOS; ELTS

Scientific Activity Research (Multiple authors)

Predictive Value of Serum and Urinary Adiponectin in Systemic Lupus Erythematosus Activity and Lupus Nephritis

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Egypt J Rheumatology and clinical Immunology 2014; 2(1):53-62.

Abstract:

Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by chronic inflammation. Lupus nephritis is a severe manifestation of SLE affecting about 50% of SLE patients with high morbidity and mortality. Adiponectin has anti-inflammatory properties. Adiponectin could be a factor linking inflammation in SLE and lupus nephritis (LN).

Aim of the work: To assess the level of serum & urinary adiponectin in SLE patients and to detect any relation between serum & urinary adiponectin levels and SLE activity and lupus nephritis.

Subjects and methods: This study included 30 female SLE patients and 15 female age matched healthy controls. SLE patients were subjected to full history taking, clinical examination and laboratory investigations of SLE & LN. Disease activity and renal involvement were assessed using SLE Disease Activity Index (SLEDAI) and Renal SLEDAI respectively. Patients were divided into active versus inactive and LN versus non-LN. Renal biopsies were taken from LN subgroup. Serum & urinary levels of adiponectin were measured using enzyme-linked immunosorbent assay (ELISA) in all subjects.

Results: Significantly higher serum & urinary adiponectin level was found in SLE patients when compared with controls. Significantly higher serum & urinary adiponectin level was found among active SLE patients when compared with inactive patients as well as among patients with LN when compared to patients without LN. Significantly higher serum & urinary adiponectin level was found among inflammatory LN class (III & IV) patients when compared to non-inflammatory LN class (I & II). Serum & urinary adiponectin had a significant positive correlation with SLEDAI, renal SLEDAI, ESR 1st hour, proteinuria, anti-ds (DNA) titre and LN class while inverse correlation with C3 titre and C4 titre, also inverse correlation between urinary adiponectin and creatinine clearance were observed.

Conclusion: Serum & urinary adiponectin levels are elevated in SLE patients and strongly associated with lupus activity & LN, so they may consider promising biomarkers for prediction of SLE activity & renal involvement especially urinary adiponectin in lupus nephritis.

Key words: Systemic lupus erythematosus, adiponectin, lupus nephritis

Scientific Activity Research (Multiple authors)

Pulmonary hypertension in adult Egyptian patients with β -thalassemia major: correlation with natural anticoagulant levels

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Tanta Medical Journal 2015, 43(2):52–59

Abstract:

Background/aim: Thalassemia constitutes a heterogeneous group of inherited anemia. In Egypt, 1000/1.5 million live births per year suffer from thalassemia. β -Thalassemia major (β -TM) is characterized by absent or reduced synthesis of β hemoglobin chains. The incidence and pathophysiology of pulmonary hypertension (PH) in patients with β -TM is not clear. The hypercoagulable state in thalassemia enhances the risk of thrombosis, such as pulmonary embolism. The aim of the present study was to investigate the prevalence of PH in adults with β -TM and investigate the role of protein C, protein S, and antithrombin III deficiencies in the pathogenesis of PH in adults with β -TM.

Subjects and methods: Forty patients with β -TM (group I) were selected, along with 20 age-matched and sex-matched healthy individuals as controls (group II). Patients were subjected to full medical history and complete clinical examination. Plasma protein C, protein S, and antithrombin III assays were measured using ELISA. Doppler echocardiography was used for estimation of systolic pulmonary artery pressure (sPAP).

Results: PH was diagnosed in 16 (40%) patients. Significantly higher levels of sPAP were found in poorly chelated and inadequately transfused patients. Significantly lower levels of protein C, protein S, and antithrombin III were found in patients with PH. There was significant negative correlation between protein C, protein S, and antithrombin III and sPAP.

Conclusion: Significant decrease in protein C, protein S, and antithrombin III was found in β -TM, especially in patients with PH, which might suggest the role of the hypercoagulable state in the pathogenesis of PH in β -TM.

Keywords: β -thalassemia major; pulmonary hypertension; protein C; protein S; antithrombin III

Scientific Activity Research (Multiple authors)

Prevalence and significance of hepatitis B core antibodies among hepatitis B surface antigen-negative Egyptian polytransfused adult patients

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Egyptian Journal of Haematology 2015, 40:143–147

Abstract:

Background/aims: Blood transfusion is a well-established line of therapy associated with risk of infection transmission. Occult hepatitis B virus (HBV) infection is defined as the presence of HBV-DNA in the serum and/or the liver in the absence of hepatitis B surface antigen (HBsAg). Combined screening of HBsAg and hepatitis B core antibody (anti- HBe) can virtually eradicate blood-transmitted HBV. The aim of this study was to evaluate the presence of anti- HBe among Egyptian polytransfused adult patients and to determine the presence or absence of HBV-DNA in the serum samples of HBsAg-negative, anti-HBe-positive polytransfused adult patients using the polymerized chain reaction (PCR) method to assess the magnitude of occult HBV infection in these patients.

Patients and methods: This cross-sectional study included 79 polytransfused patients negative for HBsAg, HBsAb, and anti-hepatitis C virus. Patients were investigated for anti- HBe and samples of anti-HBe-positive patients were tested for HBV-DNA using real-time PCR.

Results: Among the 79 HBsAg-negative sera, anti-HBe was detected in 12 of 79 (15.19%) cases. All anti-HBe-positive sera were anti-HBs-negative. HBV-DNA was detected in five of 12 (41.67%) cases. Occult HBV infection was present in 6.33% of patients.

Conclusion: The overall prevalence of occult HBV in adult Egyptian polytransfused patients on regular blood transfusion is 6.33%.

Keywords: Occult HBV, anti-HBe, HBsAg, HBV-DNA, polytransfused

Scientific Activity Research (Multiple authors)

Hepatitis C virus: A global view

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Abstract:

Hepatitis C virus (HCV) is a global challenge; 130-175 million are chronically infected. Over 350000 die each year from HCV. Chronic HCV is the primary cause of cirrhosis, hepatocellular carcinoma (HCC), and end-stage liver disease. Management of chronic HCV is aimed at preventing cirrhosis, reducing the risk of HCC, and treating extra hepatic complications. New treatments for chronic HCV has been devoted based on direct-acting antivirals, as pegylated interferon (peginterferon) is responsible for many side effects and limits treatment access. Sofosbuvir is the first compound to enter the market with Peginterferon-free combination regimens.

Key words: Hepatitis C; Peginterferon; Sofosbuvir; Direct-acting antivirals

Scientific Activity Research (Single author)

Serum monoclonal and polyclonal free light chains in newly diagnosed Egyptian patients with diffuse large B-cell lymphoma: their impact on event-free and overall survival

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Egyptian Journal of Haematology 2016, 41:1–9

Abstract:

Background/aim: Diffuse large B-cell lymphoma (DLBCL) constitutes the largest subtype of B-cell non-Hodgkin's lymphomas. The prognostic ability of the International Prognostic Index in the era of immunochemotherapy is modest. New prognostic biomarkers are mandatory to provide new insights into the risk stratification of DLBCL. Nowadays, serum-free light chain (sFLC) assay is being applied to hematologic non-plasma cell B-cell lymphoid malignancies. The aim of our work was to investigate the prevalence and prognostic value of elevated sFLC (monoclonal and polyclonal) in DLBCL and their impact on event-free survival (EFS) and overall survival (OS).

Patients and methods: This cohort study included 58 patients with DLBCL. Pretreatment serum samples were taken to detect κ and λ sFLCs with enzyme-linked immunosorbent assay. Patients were followed up every 3 months and computed tomographic scan was done every 6 months for 24 months after treatment. EFS and OS were estimated.

Results: Twenty-four patients (41.38%) had elevated κ or λ sFLC. Thirteen patients (22.41%) and 11 patients (18.97%) had monoclonal and polyclonal elevated sFLC, respectively. EFS and OS significantly decreased in patients with elevated sFLC and in those with abnormal sFLC ratio (monoclonal elevated sFLC). OS significantly decreased in patients with monoclonal elevated sFLC when compared with those with polyclonal elevated sFLC, but there was no difference between monoclonal and polyclonal elevated sFLC patients as regards EFS.

Conclusion: Elevated sFLC and abnormal sFLC ratio (monoclonal elevated sFLC) correlate with disease outcome (EFS and OS). There was no difference between monoclonal and polyclonal elevated sFLC as regards EFS but there was significant difference as regards OS.

Keywords: diffuse large B-cell lymphoma, event-free survival, monoclonal serum-free light chain, overall survival, polyclonal serum-free light chain