

calculator using age, sex, absolute lymphocyte count, bulky lymph node masses (>10cm), LDH, ECOG score and Ann Arbor stage. Data were analyzed with SPSS statistical software. Whether the prognostic scores were independent indicators or not in terms of survival and event-free survival was examined using Cox regression analysis.  $P < 0.05$  was considered significantly.

**Results:** The mean age of 103 patients in our study was  $60 \pm 9$  years and in 48% of them had extranodal disease, 64% of the patients had advanced disease, 24% of the patients had solid disease. In 37% of the patients ECOG score was  $\geq 2$ . 38% of the cases were dead. NCCN-IPI was the most successful prognostic model to predict EFS24 in the patients ( $p < 0.001$ ). While IPI24 was statistically significant to predict EFS24 ( $p = 0.03$ ), IPI was not sufficient ( $p = 0.13$ ) (Table 1A). While the best prognostic model was NCCN-IPI to predict the overall survival in 24 months ( $p < 0.001$ ), IPI and IPI24 were insufficient (with order  $p = 0.08$ ,  $p = 0.7$ ) (Table 1B). To predict the overall EFS and overall survival in the patients, the best prognostic model was NCCN-IPI ( $p < 0.001$ ), but IPI and IPI24 were insufficient ( $p > 0.05$ ) (with order Table 1C-D).

**Summary/Conclusions:** In DLBCL patients before treatment, while NCCN-IPI was superior to IPI 24 as a prognostic scoring system to predict EFS24, IPI was insufficient. Similarly to predict overall survival, NCCN-IPI was the best prognostic model. Due to the mean age of our patients was high and the number of the patients was not enough IPI24 could be insufficient when compared to NCCN-IPI to predict EFS24 and overall survival. It would be useful to do more studies to show the effectiveness of IPI24 for determining the risk factors before the treatment on DLBCL patients.

## PB1722

### EFFICACY OF SPLENECTOMY IN DIFFUSE LARGE CELL LYMPHOMA

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**Background:** Diffuse large cell lymphomas (DLCL) are often associated with splenomegaly. Large-size spleen causes both abdominal discomfort, cytopenia, regional portal hypertension and a decreased efficacy of chemotherapy. This is why splenectomy is indicated in such cases.

**Aims:** To retrospectively analyze the efficacy of splenectomy in patients with diffuse large B-cell lymphoma (DLBCL) and diffuse large T-cell lymphoma (DLTCL).

**Methods:** 43 patients with DLBCL and two patients with DLTCL underwent splenectomy.

**Results:** Splenectomy was performed in 25 male and 18 female patients aged 25-76 years with DLBCL. Indications for splenectomy included splenomegaly (in all patients), hypersplenism (anemia, leukopenia, thrombocytopenia) – in 25 patients (58.1%), regional portal hypertension – in 20 (46.5%) patients; inefficacy of chemotherapy – in 18 (41.9%) patients, and concomitant autoimmune hemolytic anemia (warm type) – in two patients. Splenectomy proved effective in 40 (93%) patients with DLBCL: abdominal syndrome, anemia and leukopenia were reverted, hemolysis in AIHA relieved, and the platelet count was normalized in patients with concomitant thrombocytopenia. The following complications were observed postoperatively: bilateral pneumonia (1 patient), chronic adrenal insufficiency (3 patients), acute thrombophlebitis of superficial veins of the right leg (1 patient), acute pancreatitis (4 patients), and thrombosis of residual limb of the splenic vein (3 patients). One patient died immediately following splenectomy. This lethal outcome was caused by acute cardiovascular insufficiency, which developed within 4 days after operation. Splenectomy did not prove effective in patients with DLBCL. The surgery did not result in normalization of concomitant cytopenia in one female patient who died within 1 month after splenectomy due to both progression of illness and chronic adrenal insufficiency. Another female patient achieved a short-term recovery following surgery (hemoglobin level as well as leukocyte and platelet count normalized) but she developed a cytopenia after 30 days and passed away due to a rapid deterioration of illness and multi-organ insufficiency. As shown by a retrospective analysis of long-term results of splenectomy in patients with DLBCL, the overall survival post splenectomy reached 63.9 months, and the mean treatment-free survival reached 36.8 months. 11 patients did not require administration of chemotherapy following splenectomy at all. 17 patients with DLBCL (39.5%) developed a relapse of illness at different timepoints after surgery. Splenectomy was performed in two patients with DLTCL. In both cases, surgical treatment proved ineffective, and the patients died within 1 month following intervention due to a relapse of cytopenia, rapid deterioration of illness and multi-organ insufficiency.

**Summary/Conclusions:** Splenectomy remains to be an effective treatment option in non-Hodgkin lymphomas. In DLBCL, the surgery helps relieve both abdominal discomfort and hypersplenism; symptoms of regional portal hypertension alleviate; there is less or no need in administration of chemotherapy; and there is no more hemolysis in concomitant AIHA. In DLTCL, splenectomy is ineffective and should be thus avoided.

## PB1723

### DONOR-TRANSMITTED TRIPLE-HIT LYMPHOMA IN A RENAL ALLOGRAFT RECIPIENT

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**Background:** Donor cancer transmission is a rare long-term complication of kidney transplantation that carries an estimated risk of approximately 0.05%. Diagnosis and management of these malignancies are difficult because of their rarity and the need for an individualized approach to treatment. CM is a 30-years-old man with a medical history significant for chronic kidney disease who underwent kidney transplantation in May 2015 with his mother as the donor. In July 2015, the donor presented with an abdominal mass diagnosed as a triple-hit lymphoma (THL), a subset of highly aggressive B-cell lymphomas characterized by the overexpression of MYC, BCL2 and BCL6. Initial staging with PET/CT and bone marrow biopsy showed widespread disease with no marrow involvement, while circulating tumor DNA (ctDNA) assay confirmed a clonal B-cell proliferation. Analysis of ctDNA was performed on recipient's plasma, but ctDNA levels were undetectable. In September 2015, CM developed a perigraft mass that was identified as a THL as well. The peculiar clinical presentation and the histochemical similarities of the two THLs raised the suspicion that the same lymphoma had been transmitted from the donor to the recipient during the transplant procedure.

**Aims:** This case describes donor transmission of THL with kidney transplantation and points out difficulties in diagnosis and management.

**Methods:** Lymphoma biopsy specimens from both donor and recipient were obtained and prepared for histological and immunohistochemical (IHC) studies and stained for the identification of Ki67, CD20, BCL6, BCL2, MYC, CD10, MUM1/IRF4, CD5, cyclin D1, CD3, EBV-LMP1 and TdT. DNA was extracted from the biopsies of both donor and recipient THL with standard methods. Samples were assessed for nine microsatellite loci and a segment of the X-Y homologous gene amelogenin by PCR with use of a kit for chimerism determination. Fluorescent in-situ hybridization (FISH) studies were performed on specimen sections using probes for sex determination. B-cell clonality analyses targeting the IGH gene for rearrangements were conducted on ctDNA obtained from plasma of both donor and recipient and from the recipient's bone marrow.

**Results:** Histology and IHC showed identical findings in both donor and recipient. In particular, MYC, BCL2 and BCL6 were positive and the proliferative index was more than 90%. FISH recognized an XX pattern in both samples. Microchimerism analysis pointed out that the donor and the recipient biopsies had identical profiles considering discriminant alleles and amelogenin (see Figure 1). Moreover, the recipient sample profile was significantly different from his basal allelic profile obtained from peripheral lymphocytes at the time of the diagnosis. B-cell clonality in the donor sample was detected at the time of the diagnosis, however ctDNA levels assessed on recipient's sample were undetectable. The same clonal band was persistently detected by ctDNA analysis of the recipient plasma and bone marrow only after September 2015.

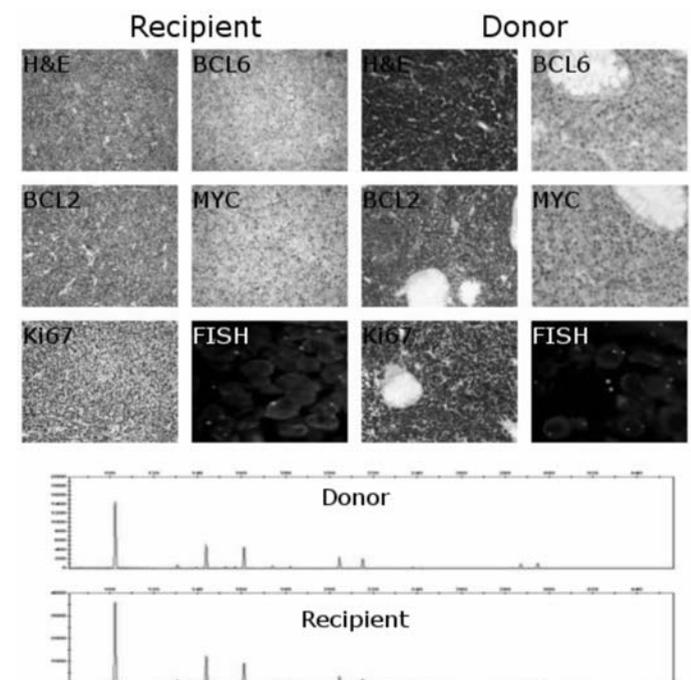


Figure 1.

**Summary/Conclusions:** We describe the transmission of a highly aggressive B-cell non-Hodgkin lymphoma by kidney transplantation. The THL was transplanted along with the renal graft, while immunosuppressive therapy and immunological impairment enabled its growth and expansion. The patient went on to complete the full course of 2 cycles of R CODOXM/IVAC and associated withdrawal of immunosuppression achieving a complete remission and preserving graft function. The donor underwent the same intensive regimen and achieved a complete response as well.

#### PB1724

#### TREATMENT OF C-MYC/BCL2 DOUBLE EXPRESSER DLBCL WITH R-CHOP CHEMOIMMUNOTHERAPY: AN AUSTRALIAN SINGLE CENTRE EXPERIENCE

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**Background:** Co-expression of c-myc and BCL2 in Diffuse Large B-cell Lymphoma (DLBCL), (increasingly known as 'double expresser' DLBCL), is associated with inferior outcome with standard-of-care R-CHOP immunochemotherapy.

**Aims:** To retrospectively identify patients with 'double expresser' immunophenotype within our patient cohort of DLBCL, and to analyze their outcomes following treatment.

**Methods:** Chart review of patients with DLBCL treated with RCHOP chemoimmunotherapy between 2007 and 2014 at our institution. We retrospectively performed immunohistochemical staining for c-myc and BCL2 on pre-treatment tumor tissue blocks to identify patients with 'double expresser' immunophenotype. Other prognostic factors including the revised international prognostic index (R-IPI) score, initial bulky disease (>7.5cm) and cell of origin were also recorded and analyzed. Progression-free survival (PFS) were analyzed using Kaplan–Meier curves and statistically tested with the Gehan-Breslow-Wilcoxon test. 2-tailed chi-square test was used to compare incidence of various prognostic factors in subgroup analysis.

**Results:** 89 patients were included in the study. Patients with high risk R-IPI score, bulky disease, and elevated serum lactate dehydrogenase level (LDH) showed reduced progression-free survival ( $p=0.03$ ,  $p=0.04$ ,  $p=0.002$  respectively). In particular, LDH above 2 times of upper limit of normal (ULN) was associated with a 56% reduction in PFS. There was no significant difference in PFS between 'germinal center' and 'non-germinal center' cell of origin subtypes of DLBCL. 34 patients were found to have 'double expresser' immunophenotype. They showed a higher rate of disease progression (32% vs 16%,  $p=0.03$ ), than the remaining DLBCL patients, with progression occurring predominantly within 24 months of treatment. The 'double expresser' subgroup also had a higher incidence of bulky disease (50% vs 13%,  $p=0.01$ ), and LDH above 2xULN (35% vs 11%,  $p=0.005$ ), at presentation. All patients with normal LDH levels and non-bulky disease ( $n=7$ ) remained in remission at a median follow-up of 32 months (Figure 1).

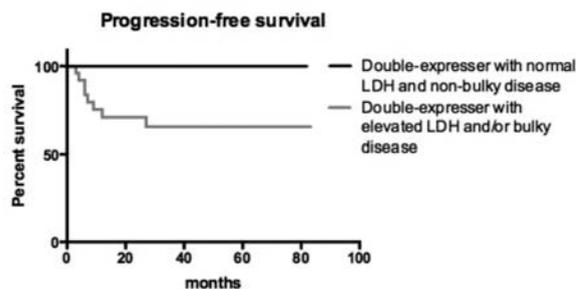


Figure 1.

**Summary/Conclusions:** We present a small single center series of 'double expresser' DLBCL. Patients with the double expresser phenotype had a higher incidence of bulky disease and markedly elevated LDH level, which was associated with higher risk of disease progression. Knowing this, it may be reasonable to adopt a more intensive treatment approach for these patients. Interestingly, having a normal LDH level at diagnosis and absence of bulky disease (known good prognostic factors) retained their protective influence even in patients with 'double expresser' phenotype.

#### PB1725

#### METRONOMIC CHEMOTHERAPY IMPROVES SURVIVAL IN RESPONDING PATIENTS WITH RECURRENT/REFRACTORY LYMPHOMA

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**Background:** Metronomic chemotherapy (MC) consists of continuous administration of oral chemotherapy at low, potentially less toxic doses without prolonged drug-free breaks. MC might be a useful for many patients with recurrent or refractory lymphomas that are unable to tolerate intensive therapies.

**Aims:** The aim of this study was to retrospectively analyze the efficacy and toxicity of MC in recurrent or refractory lymphomas in our Institution.

**Methods:** Retrospective analysis of patients with lymphoma treated with MC from 2009 to 2014 in our Institution. The metronomic scheme consisted of oral 50 mg of prednisone, 50 mg of cyclophosphamide, 50 mg of etoposide, and/or 50 mg of procarbazine evenly distributed throughout the day. Clinical response, duration of response, progression-free survival (PFS) and overall survival (OS) was evaluated. Clinical response was defined as improvement of the symptoms of lymphoma and/or shrinkage of tumours (lymph nodes or affected organs) by physical examination and/or imaging.

**Results:** *Patient demographics and characteristics:* 28 lymphoma patients consecutively treated with MC were included. 10 patients had diffuse large B-cell lymphoma (DLBCL), 6 cutaneous T-cell lymphoma (CTCL), 5 peripheral T-cell lymphoma (T-NHL), 4 Hodgkin lymphoma (HL), 1 mantle cell lymphoma, 2 other types of non-Hodgkin lymphoma. Median number of prior regimens was 3 (range 1-8). 26 patients (93%) had refractory disease to prior treatment.

*Efficacy:* Clinical response was observed in 23 patients (82%) with a median duration of response 6 months (95% CI, 0-11 months). No differences were found in clinical response rate, duration of response, PFS and OS among the aggressive or indolent lymphomas. With a median follow-up of 14 months, median OS was 6 months. Of note, responders to MC showed a significantly increased OS (median OS of 11 months in responders vs 1 months in non-responders ( $p<0.001$ ) (Figure 1). Remarkably, PFS was also significantly higher in responders, 42% of cases were progression-free at 6 months in responders vs 0% in non-responders ( $p<0.001$ ). Twenty patients died: progressive disease ( $n=15$ ), infection ( $n=4$ ) and non-related ( $n=1$ ). *Toxicity:* Seventeen patients (61%) had adverse events grade 3/4, mainly hematologic. A total of 6 patients had infections grade  $\geq 3$ : urinary tract infection ( $n=2$ ), pneumonia ( $n=2$ ), multiresistant *Pseudomonas aeruginosa* bacteremia+Cytomegalovirus infection ( $n=1$ ) and *Escherichia coli* sepsis ( $n=1$ ). The main cause of treatment discontinuation was progressive disease. Only one gastrointestinal adverse event grade 4 led to MC discontinuation (3.6%). Dose modifications of MC drugs was performed in 15 patients (54%) and 12 patients required use of granulocyte colony stimulating factor (G-CSF). 54% of patients received cotrimoxazole as primary or secondary prophylaxis.

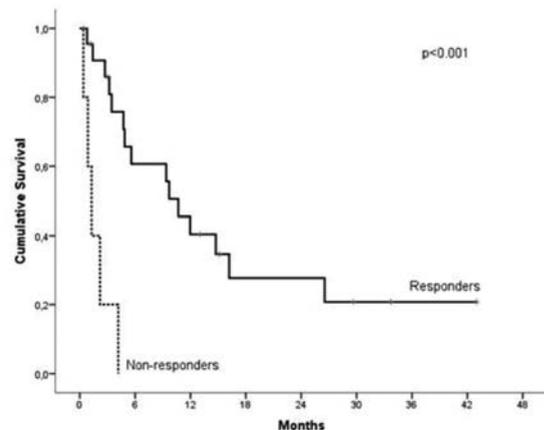


Figure 1.

**Summary/Conclusions:** Our study supports the anti-tumor activity of MC in patients with advanced lymphoma chemo-resistant and relapsed to multiple therapies with no other therapeutic alternatives. Clinical responses were observed in all lymphoma subgroups and the toxicity profile was acceptable, even in heavily pretreated patients. Even most of our cases had been considered refractory to prior treatment, responding patients to MC had an improved PFS and even OS.

#### PB1726

#### RELATIVE TOTAL DOSE INTENSITY OF TREATMENT WITH R-CHOP IN OBESE VERSUS NON OBESE LYMPHOMA PATIENTS DOSED ON ACTUAL BODY WEIGHT: A SINGLE CENTRE EXPERIENCE

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**Background:** The number of obese patients in the UK is growing to epidemic