Results: The cohort consists out of 67 pts. with median age 49 years (21-69), 61% men, high LDH in 90%, intermediate-high and high aa-IPI risk resp. in 54% and 37% pts. resp. (there were only 7% low/low-intermediate risk pts). There were 52% of non-GCB and 48% of GCB patients, and 24% of DE and 76% of nonDE. ASCT was planned in 73% of patients (66% with MegaCHOP+/–ESHAP regimen) and response driven (PR only) after R-CHOP induction in 27% pts. PET before ASCT was performed in all pts. and was negative in 69%, positive in 25% and inconclusive in 6% pts. With median follow-up 6.5 years, the 7-year probability of PFS and OS was 76% and 81%. There was no PFS difference between DE and non-DE (HR 1.3; 0.44-4.01; p ns; 63.8% vs 78.2%, at 7 y) nor OS difference (HR 0.51; 95% CI 0.17-1.93; p ns; 86.5% vs 77.9%, at 7 y) (Figure 1). There was also no PFS difference between GCB and non-GCB (HR 1.02; 95% CI 0.39-2.66; p ns; 75% vs 74.8% at 7 y) nor OS difference (HR 1.6; 95% CI 0.56-4.61; p ns; 74.9% vs 85% at 7 y). In this cohort, preASCT PET positivity was not predictive for significantly worse PFS (HR 1.59; 95% CI 0.52-5.55; p ns; 70.6% vs 78.9% at 7 y) or OS (HR 1.45; 95% CI 0.42-5.75; p ns; 76.5% vs 84.1% at 7 y).

Conclusions: Double-expressor DLBCL had no worse outcome vs non-DE in the cohort of consecutively treated high-risk pts, when HDT and autologous stem-cell transplant were used as part of the first-line treatment. This observation suggests that in clinically high-risk young patients, the impact of double BCL2 and MYC expression is reduced, and/or intensive immunochemotherapy with ASCT could overcome it.

Keywords: “double-hit” lymphomas; autologous stem-cell transplan- tation (ASCT); diffuse large B-cell lymphoma (DLBCL)

196 DOUBLE-EXPRESSOR LYMPHOMAS DO NOT HAVE INFERIOR OUTCOME AFTER AUTOLOGOUS STEM-CELL TRANSPLANT IN THE FIRST LINE TREATMENT


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Introduction: Small subgroup of double-hit (DH) or larger one of double-expression (DE) diffuse large B-cell lymphomas (DLBCL) were shown to have worse outcome compared to non-DH and non-DE lymphomas. It has been demonstrated that intensive treatment and high-dose therapy (HDT) with ASCT could improve the results compared to standard treatment. Relapsed/refractory DE DLBCL have however still inferior PFS after ASCT (Herrera, JCO 2016). We have performed the analysis of DE DLBCL patients (pts.) who were transplanted as part of the first-line treatment and compared them to the transplanted non-DE DLBCL pts.

Methods: Eligible for the analysis were consecutive pts. with DLBCL not otherwise specified, diagnosed in single center between 2002 and 2015, treated with rituximab and anthracycline-based chemotherapy who underwent HDT and ASCT as part of the first-line therapy either planned (R-MegaCHOP/ESHAP/BEAM or PET-RIMCEB study GovTrial No: NCT00558220) or pts. who underwent ASCT because of partial remission (PR) only at the end of the induction. Only pts with tissue blocks available for histopathological review (VC, RJ, JS, LB) were eligible for analysis. Cell of origin (COO) was examined by immuno-histochemistry (Hans 2004); for MYC and BCL2, all patient were scored semiquantitatively in 10% increments with cutoff values of 40% for MYC and 70% for BCL2. Pearson chi-square, Mann-Whitney, Kaplan-Meier and log rank tests were used.

Conclusions: This large retrospective study showed that reduced toxicity myeloablative fludarabine/busulfan regimens did not improve outcome of adults allografted for NHL. FB2 conditioning regimen still should be considered as the standard of care conditioning regimen in this setting.

Keywords: allogeneic stem-cell transplant (alloSCT); busulfan; non-Hodgkin lymphoma (NHL)

197 DIRECT-ACTING ANTIVIRALS DURING OR AFTER IMMUNO-CHEMOTHERAPY IN HEPATITIS C VIRUS-ASSOCIATED DIFFUSE LARGE B-CELL LYMPHOMAS


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Introduction: Direct-acting antivirals (DAAs) demonstrated >90% sustained virological responses (SVR) across all genotypes in hepatitis C virus (HCV)-infected patients (pts), without significant side effects. Updated international guidelines suggest HCV eradication by DAAs in pts with HCV+ diffuse large B-cell lymphoma (DLBCL) achieving complete response (CR) after 1st line immunochemotherapy (I-CT), although limited experiences substantiate this recommendation. Moreover, no data concerning concurrent administration of DAAs with I-CT have been reported.

Methods: We retrospectively analyzed virological and hematological outcome and survival of 32 consecutive pts with HCV+ DLBCL treated at 16 centers with DAAs regimens either concurrently (Concurrent Cohort, ConC: n = 7) or subsequently (Sequential Cohort, SeqC: n = 25) to 1st line I-CT.

Results: Thirty-one pts had de novo DLBCL (5 with low-grade component) and 1 transformed marginal-zone lymphoma. Germinall-center (GC)/non-GC cases according to Hans were 37/63%. Median age was 62 years (33-80), stage was III/IV in 28 pts (87.5%), IPI high/ high-intermediate in 15 pts (47%). Extranasal sites were involved in 18 pts (56%) (liver in 8 and kidney in 4), spleen in 16 (50%) and bone marrow in 10 (31%). Genotype was 1 in 20 (63%), 2 in 10 (31%) 3 and 4 in 1 pt (3%). Cirrhosis was evidenced in 7 pts (22%) by liver biopsy and/or FibroScan. Seven pts (22%) previously failed interferon-based antiviral therapy (AT). I-CT was R-CHOP-like in 30 pts and R-ACVBP in 2. Anthracyclines dose was reduced in 10 pts (median 45%). I-CT was completed in all but 3 pts due to toxicity. Overall, 30/31 evaluable pts obtained CR (97%), while 1 progressed. All pts received appropriate DAAs according to genotype: 30 pts sofosbuvir (SOF)-based regimens (SOF+ledipasvir in 11, SOF + ribavirin [RBV] in 10, SOF + daclatasvir in 7, SOF + simeprevir in 2) and 2 pts ombitasvir-paritaprevir-ritonavir + dasabuvir. Median AT duration was 12 weeks (12-24). Overall, among 27 assessable pts at the time of present analysis 25 achieved SVR (93%), 4/5 (80%) in ConC and 21/22 (95%) in SeqC. The 2 non-responders achieved SVR after a 2nd DAA regimen. DAAs were well tolerated, with only 7 pts (22%) experiencing 13 grade (g) 1-2 adverse events (AEs) in SeqC (g 1 fatigue in 4, g 2 RBV-related anemia in 2 pts), while no AE was recorded in ConC. One pt treated concurrently (14%) experienced hepatic toxicity (g 4), compared to 14 pts (56%; g 1-2 in 9, g 3-4 in 5) treated sequentially (p = 0.08). At a median follow-up of 2.3 years (0.3-9.4), no pt died (OS 100%), 2 pts progressed (2 y PFS 93.2%, 95% CI: 75.4-98.3%) (Figure 1) and 1 developed hepatocellular carcinoma (2 y EFS 88.5%, 95% CI: 68.0-96.2%). IPI ≥2 extranasal sites and albumin <3.5 g/dl retained prognostic value on PFS (p < 0.01).

Conclusions: Excellent outcome of this selected retrospective series suggests benefit of HCV eradication by DAAs either after or during I-
CT in HCV+ DLBCL. Moreover, concurrent DAAs and R-CHOP administration resulted feasible and effective and may prevent hepatic toxicity of I-CT.

**Keywords**: diffuse large B-cell lymphoma (DLBCL); hepatitis C

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**CURRENT THERAPY OF SECONDARY CNS INVOLVEMENT IN MALIGNANT LYMPHOMA: DATA FROM A MULTICENTER PROSPECTIVE INTERNATIONAL REGISTRY**

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**Introduction**: CNS involvement is a rare complication of systemic lymphoma. With conventional therapy, the prognosis of secondary CNS lymphoma is poor with median overall survival (OS) in most series of approx. 6 months. The optimal therapeutic management has not been established thus far.

**Methods**: Since 2011, 181 patients have been included in an ongoing prospective international registry. Here, data of the first 173 patients included until November 2016 is presented.

**Results**: 30 patients had CNS involvement at diagnosis (cohort I) and 143 at progression/relapse (cohort II). The median age was 63 years (26-86). Of 155 patients with complete data available, 122 (79%) had aggressive B-cell lymphoma, 25 (16%) indolent lymphoma, 5 (3%) mantle cell lymphoma and 3 (2%) T-cell lymphoma. Simultaneous systemic involvement was found in 42% of patients in cohort II. Therapy for CNS involvement and outcome was analyzed in 99 patients thus far (16 in cohort I and 83 in cohort II). Systemic therapy alone was given to 48 (49%), systemic + intrathecal therapy to 43 (43%), intrathecal therapy alone to 5 (5%), radiotherapy alone to 2 (2%); one patient did not receive any treatment. Systemic chemotherapy was high-dose methotrexate (HDMTX)-based in 81 (89%) and high-dose cytarabine (HD AraC)-based in 53 (58%); 61 (61% of all) patients received rituximab systemically. Liposomal cytarabine was the most frequent intrathecal therapy given in 30 out of 48 patients (63%). High-dose chemotherapy followed by autologous stem cell transplantation (HD-ASCT) was performed in 25 (25%) patients. The median progression-free survival (PFS) was 5.9 months (95% CI 3.1-8.7), the median OS 18.6 months (95% CI 10.3-26.9). On univariate analysis, CNS lymphoma at diagnosis, no meningeal involvement, better ECOG performance status, treatment with rituximab, HD-ASCT and response to therapy were associated with better outcome. On multivariate analysis, a prognostic role for CNS involvement at first diagnosis and HD-ASCT (for OS) and no meningeal involvement (for both PFS and OS) was found with response to CNS therapy being the dominating prognostic factor (for both OS and PFS).

**Conclusions**: This is the largest prospective series on SCNSL in the era of modern lymphoma therapies. Our results suggest that with intensive HDMTX- and HD AraC-based chemotherapy, the outcome of