Autologous transplant

250 EFFECT OF DURATION OF FIRST REMISSION ON LONG-TERM OUTCOME OF HODGKIN LYMPHOMA PATIENTS UNDERGOING HIGH-DOSE THERAPY AND AUTOLOGOUS STEM-CELL TRANSPLANTATION (HD-ASCT)

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Background: Duration of first remission (DOR) of Hodgkin lymphoma (HL) affects outcome after HD-ASCT. Those who relapse < 12 mos after completion of primary therapy do worse than those who relapse > 12 mos. Since 1985, HD-ASCT has been recommended in British Columbia (BC) for all HL patients (pts) relapsing after primary therapy, irrespective of time to relapse. We evaluated the impact of DOR on long-term outcomes.

Methods: We reviewed all HL pts who underwent HD-ASCT for progression after primary chemotherapy +/- radiation. We used the DOR from the end of primary therapy to the date of first progression to identify 4 groups: primary progression (PP) (progression during or within 3 mos of completion of primary therapy); early relapse (3 to <12 mos); late relapse (12 to <48 mos); very late relapse (≥ 48 mos).

Results: 242 pts were identified: male, 53%; median age at diagnosis, 28 y (range 16-59) and at HD-ASCT, 31 y (range 31-62); advanced stage at diagnosis (stage IIB, II bulky, III or IV), 94%; stage 3-4, 61%; B symptoms, 21%; bulky disease (≥10 cm), 42%; primary therapy: ABVD/ABVD-like, 97%; MOPP-like, 3%; combined modality therapy, 31%. PP occurred in 87 pts (36%), early relapse in 77 (32%), late relapse in 56 (23%) and very late relapse in 22 (9%), including 2 who relapsed after >10 y. Secondary therapy prior to transplant included COP/COPP (23%); GDP (26%); MVPP (25%); no treatment (22%); other (4%). Conditioning regimen was CBV in the majority of cases (87%); BEAM (11%); other (2%).

At a median follow-up of 9 y (range 0.1-24), 131 pts (54%) are alive free of HL; 86 pts (36%) have relapsed. For all pts, median overall (OS) and progression free survivals (PFS) are 18.6 y (CI 14.7-22.4) and 17 y (CI 6.5-28), respectively. 13 pts (5.3%) died of complications related to transplant, 5 (2%) from secondary malignancies and 7 (3%) from unrelated causes. For the 86 pts who relapsed after HD-ASCT, median OS is poor (11 mos, CI 0-32).

DOR significantly affected OS for the PP, early, late or very late relapse groups: 15 y OS 44%, 65%, 77%, 82%, respectively (p<0.001) and 15 y PFS 35%, 58%, 64%, 71%, respectively (p<0.001). Pts with PP have much worse OS and PFS, median, 5.7 y and 1.2 y, respectively. Pts in the early and late relapse groups (3-12 mos vs 12-48 mos) have quite similar OS (p=0.33) and PFS (p=0.44); however, those in the very late relapse group (≥ 48 mos) show a strong trend to improved TTP (time to progression) (P=0.072) when compared to the pooled early and late groups. In this very late relapse group, only 1 pt died of HL, while 2 are alive after a second relapse (9%) and 3 died of secondary malignancies.

Conclusion: In this large uniformly treated cohort of HL pts with long-term follow-up, post-transplant outcomes improved with longer duration of first remission. In particular, pts who relapsed very late had excellent outcomes, with long-term survival over 80%. HD-ASCT should be the treatment of choice in all transplant-eligible pts, regardless of time to relapse.

251 THE GERMINAL CENTER (GCB)/ ACTIVATED B-CELL (ABC) SUBCLASSIFICATIONS HAVE A PROGNOSTIC IMPACT FOR RESPONSE TO SALVAGE THERAPY IN RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL). THE BIO-CORAL STUDY

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Introduction: Cell of origin (COO) has a major prognostic impact in DLBCL. Our purpose was to evaluate the prognostic value of COO using various immunohistochemical algorithms as well as gene expression analysis in relapsed/refractory DLBLC in patients prospectively treated and randomized between R-DHAP or R-ICE followed by intensive therapy plus autologous stem cell transplantation, i.e. the CORAL trial.

Methods: Histological material was available in a total of 249 patients at diagnosis (n= 189 cases) and/or at relapse (n= 147 cases), including 87 matched pairs. The cases were analysed by immunochemistry for CD10/MME, BCL6, MUM1/IRF4, FOXP1, and BCL2 expression and by FISH for *BCL2*, *BCL6* and *c-MYC* breakpoints. GEP was performed in a subset 39 patients.

Results: Tumor immunophenotype and chromosomal abnormalities were statistically highly concordant in the biopsies at diagnosis and at relapse within the matched pairs. GCB phenotype based on Hans algorithm and on GEP was significantly associated with a better PFS, but only in the R-DHAP arm. In multivariate analysis independent prognostic relevance was found for GCB/non-GCB Hans phenotype interaction with the treatment (p=0.04), prior rituximab exposure (p=0.0052), secondary aaIIPI (p=0.039), and FoxP1 expression (p=0.047).

Conclusion: COO remains a major and independent factor in relapsed patients, with a better response to R-DHAP salvage chemotherapy in GCB-like DLBCL. Treatment of ABC subtype is still unsatisfactory.

252 INFLUENCE OF PRIOR EXPOSURE TO RITUXIMAB ON RESULTS OF AUTOLOGOUS STEM-CELL TRANSPLANTATION IN PATIENTS WITH RELAPSED OR REFRACTORY AGGRESSIVE B-CELL LYMPHOMA: SINGLE-CENTRE EXPERIENCE

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Background: Recent studies indicate that the use of highly effective rituximab (R)-containing primary therapy in Diffuse Large B-cell Lymphoma (DLBCL) makes it more difficult to salvage patients who are refractory or who relapse. To date, autologous stem-cell transplantation (ASCT) is the reference treatment for these patients, but the impact of the use of R in combination with chemotherapy on the ulterior results of ASCT is still unknown.

Patients and Methods: We have retrospectively analysed 106 patients (pts) with DLBCL (n=92) or follicular grade 3 lymphoma who consecutively received ASCT as salvage therapy at our centre between May 1990 and September 2010. Median age was 51 years (14-70). The analysis was performed according to whether patients had (n=51, ''R+'' group) or had not (n=55, "R-" group) received R prior to ASCT.

Results: Overall response (OR) rate to ASCT was 85%, with 85 pt (80%) achieving complete response (CR) and 5 (5%) partial response (PR). Pts in the R+ group had higher CR (92% vs 69%, p=.003) and OR (81% vs 67%, p=.045) rates than pts in the R- group. In multivariate analysis, factors with significant influence on CR rates were: sex (female), disease status at transplant (CR), number of prior chemotherapy lines (<3), and prior exposure to R (yes). The median follow-up was 42 (2-113) and 97 (2-219) months in the R+ and R- groups, respectively. Patients in the R+ group had a significantly better progression-free survival (PFS) (72% vs 52% at 5 years, p=.048) and overall survival (OS) (85% vs 61% at 5 years, p=.02) as compared with patients in the R- group. In multivariate analysis, independent factors with significant influence on both PFS and OS were prior exposure to R, year of transplant > 2000 and response to transplant. Analyzing separately the R+ group, both PFS and OS were better in patients who received R with the first-line therapy (83% and 93% at 5 years, respectively) than in patients treated with R only in the salvage setting (53% and 70%, respectively), although the differences did not reach statistical significance (p=.09 and .06, respectively).

Conclusions: Our retrospective single-centre analysis indicates that ASCT is an effective option for patients with relapsed or refractory aggressive B-cell lymphoma pre-treated with R-containing first-line or salvage chemotherapy, mainly for those who are on CR before the transplant.

253 HIGH DOSE CHEMOTHERAPY FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) MAY OVERCOME ADVERSE PROGNOSIS IN PATIENTS WITH DIFFUSE LARGE B CELL LYMPHOMA (DLBCL) WITH AN ACTIVATED B CELL (ABC) MOLECULAR PROFILE

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The genomic expression profiling of DLBCL into ABC and Germinal Center B Cell (GCB) has divided patients into two groups with dramatically different prognoses. We explored the effect of ASCT on the outcome of patients with relapsed DLBCL and unknown molecular subtype. We performed a retrospective review from Jan 1999-Jan

2008 of patients with relapsed/refractory DLBCL that underwent ASCT. We analyzed diagnostic biopsies with TMAs using the Hans algorithm. We excluded patients with other lymphomas, insufficient tissue or incomplete data. The Chi squared test and the Kaplan-Meier method was used for statistical analyses. We identified 37 patients with relapsed/refractory DLBCL that fit the above criteria. 17 patients were excluded by the above mentioned criteria. Of the remaining 20 patients; 13(65%) were ABC type and 7(35%) were of the GCB type. Median age of all patients was 52 yrs (44% > 60 yrs in the ABC group and 42% in GCB group). There was no statistically significant difference between patient characteristics in both groups. Only 1 patient in each group had a high IPI score, the rest were low and low-intermediate. 69% of patients in the ABC group and 57% of the GCB group had a CR to first line chemotherapy. 46% of the ABC group and 42% of the GCB group had Relapse-1 sensitive disease at ASCT. Only 2 patients (both ABC group) had primary refractory disease. 53% of patients in the ABC and 71% of patients in the GCB groups were greater than 24 months from their diagnosis to the time of ASCT. The median follow-up of surviving patients was 48 months (23 –69 months). The median EFS for patients with a GCB profile was 48 months, while the median EFS in the ABC group has not been reached. (p = 0.84). The median OS for patients with a GCB profile is 61 months and the median OS for patients with an ABC profile is 48 months (p = 0.98). In our retrospective analysis of patients with relapsed /refractory DLBCL, 65% of patients that proceeded to a ASCT were of the ABC profile compared to 35% of patients with the GCB profile. However the GCB profile did not predict for a difference in the EFS and OS after ASCT and the median EFS for patients with the ABC profile has not been reached. This suggests that high dose chemotherapy may overcome the poor prognostic factors of the ABC profile in patients selected for ASCT and a larger multicenter study is planned to confirm these observations.

254 MINIMUM TOLERABLE INTERVAL OF ^{90}YTTRIUM IBRITUMOMAB-TIUXETAN TO AUTOLOGOUS STEM CELL TRANSPLANTATION AFTER HIGH-DOSE CHEMOTHERAPY WITH CARMUSTIN, ETOPOSIDE, CYTARABINE, MELPHALAN IS 10 DAYS. FIRST RESULTS FROM DSHNHL ESC Z-BEAM TRIAL FOR RELAPSED OR REFRACTORY AGGRESSIVE B-NHL

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High-dose therapy (HDT) and autologous stem cell transplantation (ASCT) is significantly less effective in patients with aggressive B-cell lymphoma if first-line therapy included rituximab (Gisselbrecht et al. JCO 2010). Combining BEAM with radioimmunotherapy (Zevalin®) is a promising option to enhance the efficacy of the high-dose regimen. Patients (pts) without disease progression during salvage therapy of relapsed or refractory CD20+ aggressive B-cell lymphoma were included in this prospective, multi-centric, phase I/II trial. Primary endpoint was the maximum tolerated dose of Zevalin® given closest to HDT defined as <2 pts with dose limiting toxicity or treatment-related mortality in a 6+6 pts cohort. First, we reduced the time interval of Zevalin® (0.4 mCi/kg body weight) to ASCT from 14 to 12 and then 10 days. Subsequently it was planned to increase the Zevalin® dose. From 2006 to 2009 26 pts, median age 58y (34-66) received study drug. Histology included 14 DLBCL, 6 FL III°, 5 transformed FL and one aggressive B-cell lymphoma without further subtyping. 25/26 pts first-line therapy contained rituximab. Median lines of prior therapies were 1 (1-4). Median interval from diagnosis to relapse or progression was 16 months, with 11 pts progressing within one year after diagnosis. IPI at time of relapse was 0-1 in 12 pts, 2-4 in 14 pts. 9/26 pts achieved CR after salvage therapy and 20/26 pts after Z-BEAM. Median CD34+ cell dose was 4.2x10e6/kg (2.1-19). Engraftment showed no significant differences in pts of different cohorts. Median recovery of leukocytes (>1/nl) and platelets (>25/nl) were at day +10 and +13. Two therapy-related early deaths (day +7, +18) occurred due to infections. Zevalin® (0.4 mCi/kg body weight) at day -10 of ASCT was determined as minimum tolerated interval of radioimmunotherapy to ASCT after BEAM. Median follow-up is 18 months. 3-y PFS and OS is 59% and 73%, respectively. Z-BEAM followed by ASCT was safe and feasible and results in a high response rate in rituximab pretreated patients with aggressive B-cell lymphoma. Extended studies at the maximum tolerated dose are warranted.

255 A NEW HIGH DOSE THERAPY STRATEGY WITH BENDAMUSTINE IN ADJUNCT TO ETOPOSIDE, CYTARABINE AND MELPHALAN (BEEAM) FOLLOWED BY AUTOLOGOUS STEM CELL RESCUE IS SAFE AND HIGHLY EFFECTIVE FOR THE TREATMENT OF RESISTANT/RELAPSED LYMPHOMA PATIENTS: A PHASE I-II STUDY ON 44 PATIENTS

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Background: We designed a phase I-II study to evaluate the safety and the efficacy of Bendamustine for the conditioning regimen to ASCT for resistant/relapsed lymphoma patients. As biological background, we performed in vitro experiments showing the synergistic activity of bendamustine with etoposide, aracytin and melphalan in lymphoma cell lines.

Matherials and Methods: 44 patients (median age 47 years) with resistant/relapsed non-Hodgkin (29) or Hodgkin (15) lymphoma were enrolled. The new regimen consisted of increasing doses of Bendamustine, together with fixed doses of Etoposide (200mg/m^2/day on days -5 to -2), Cytarabine (400mg/m^2 on days -5 to -2) and Melphalan (140 mg/m^2 on day -1). The starting dose of Bendamustine was 160 mg/m^2/daily given on days -7 and -6, which was escalated according to the Fibonacci's increment rule up to 200 mg/m^2. The study was registered at EMEA (EUDRACT n^o 2008-002736-15).

Results: The administration of Bendamustine was safe in the first 3 cohorts of patients; we then fixed the dose for the phase II study to 200 mg/m^2. A median number of 6.1x10^{6}CD34$^+$/kg cells was reinfused to patients. All patients engrafted. Median times to ANC>0.5x10^9/l, Plt >20x10^9/l and Plt >50x10^9/l were 10, 13 and 16 days respectively. Toxicity was mild, with only 11 patients experiencing a grade III-IV oral mucositis. After a median follow-up of 20 months from transplant, 37/44 patients (84%) are alive and disease-free (CT and PET), whereas 5/44 relapsed early after ASCT (3 months), and only 2/44 did not respond to therapy. Notably, 4/44 patients achieved the first CR after the BeEAM therapy.

Conclusions: The new BeEAM regimen is safe and highly effective in heavily pretreated lymphoma patients.

256 TARGETED INTENSIFICATION BY A PREPARATIVE REGIMEN FOR PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) UTILIZING STANDARD-DOSE YTTRIUM-90 IBRITUMOMAB TIUXETAN RADIOIMMUNOTHERAPY (RIT) COMBINED WITH BEAM FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT). GROUPE D'ETUDE DES LYMPHOMES DE L'ADULTE (GELA) STUDY Z-BEAM 2

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Introduction: To determine the safety and outcome following standard-dose Yttrium-90 Ibritumomab Tiuxetan plus BEAM chemotherapy and ASCT as consolidation of front line treatment after CR/PR in patients with DLBCL.

Material and Methods: Seventy-five consecutive patients, median age 45 years (range, 19-64) with IPI 1:1pt, IPI 2:27pts or IPI 3-5:47 pts were included. After treatment with R-CHOP X 4-6 (36pts) or R-ACVBP X 4 (39pts), 71 patients received Rituximab 250 mg/m^2 on d-21, Rituximab 250 mg/m^2 followed by Y^{90} Ibritumomab Tiuxetan 0.4mCi/kg on d-14, BEAM started on d-7 followed by ASCT. Response rate (CR and PR) were defined according Cheson 1999. PET imaging was performed before ASCT in all patients. Primary endpoint was event free survival (EFS) at 2 years.

Results: Median time to reach a neutrophil count > 500/μL and platelet count > 20 000/μL was 11 days. Severe adverse events were reported in 23 cases, mostly infection (39%). There was one toxic death before day 100 due to septic shock. With a median follow-up of 23 months, the 2-yr EFS and overall survival (OS) are 74% (95% CI: 62-83%) and 80.5% (95% CI: 69-88%) respectively.

Seventeen patients (23%) presented a first progression/relapse at the time of analysis. The 2-yr DFS are 88% (95% CI: 75%-95%) in 59 pts (81%) who obtained a CR post transplant. Response CR: 59pts or PR: 12 pts before ASCT did not influenced EFS and OS. There was no different outcome between the 20 patients PET + before ASCT and PET - patients. IPI score 3-5 affected EFS, 67% (p=0.03) and OS (p=0.01).

Conclusions: Adding 90Y ibritumomab tiuxetan to high-dose BEAM is safe without an increase in transplant-related toxicity or delayed engraftment. Outcome was similar for patients with positive or negative pre-ASCT PET evaluation. Randomized study is now warranted.

257 SIGNIFICANT IMPROVEMENT IN OVERALL SURVIVAL IN HIGH-RISK AGGRESSIVE B CELL NON-HODGKIN'S LYMPHOMA AFTER ^{90}YTTRIUM IBRITUMOMAB TIUXETAN-BEAM FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION

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Introduction: High dose chemotherapy followed by autologous stem cell transplantation (AuSCT) induces long term disease free survival in 50-60% of patients with diffuse large B cell lymphoma (DLBCL) after rituximab containing (re-) induction therapy. Adding ^{90}Yttrium ibritumomab tiuxetan prior to the BEAM conditioning regimen has proven to be feasible and shows promising results with respect to disease free and overall survival in high risk DLBCL patients. At the VU University Medical center, rituximab was added to (re-)induction therapy starting July 2001. From 2006 we started to add ^{90}Yttrium ibritumomab tiuxetan (Zevalin®) to BEAM (Z-BEAM) in DLBCL patients. In this retrospective analysis we compare outcome after Z-BEAM with outcome after BEAM, both followed by AuSCT.

Patients and Methods: All high risk DLBCL patients consolidated with AuSCT in CR or PR after rituximab-containing induction therapy were included. High-risk DLBCL was defined as either relapsed or refractory DLBCL or as histological transformation of indolent NHL. AuSCT was preceded by BEAM conditioning plus the addition of ^{90}Yttrium ibritumomab tiuxetan (starting 2006: Z-BEAM group) or by BEAM only (BEAM group). EFS and OS were estimated using the Kaplan-Meier method and compared using the log rank test.

Results: 43 patients received Z-BEAM and 42 patients received BEAM conditioning. Median age was 56 and 52 years respectively. No significant differences in disease characteristics were seen. Median follow up (range) was 15 months (0-54) and 39 months (0-112) respectively. Overall survival was significantly better in the Z-BEAM group compared with the BEAM group (p=0.02) with an estimated 2 year overall survival of 90% vs. 65%. In the first 2 years of follow up 7 patients in the Z-BEAM group relapsed compared to 11 in the BEAM group, this did not reach significance (p=0.09). Time to recovery of neutrophils and thrombocytes was not significantly different. Patients who relapsed in both groups were able to receive re-induction chemotherapy and, if indicated, allogeneic SCT without being compromised by decreased bone marrow reserve or non haematological toxicities.

Conclusions: Adding ^{90}Yttrium ibritumomab tiuxetan to the BEAM conditioning regimen preceding AuSCT leads to a significant improvement in overall survival in relapsed, refractory or transformed NHL patients. Addition of ^{90}Yttrium ibritumomab tiuxetan did not result in decreased bone marrow reserve or non haematological long term sequelae enabling treatment of relapse including allogeneic SCT.

258 SYSTEMIC AND INTRATHECAL CHEMOTHERAPY FOLLOWED BY HIGH-DOSE CHEMOTHERAPY WITH AUTOLOGOUS STEM CELL TRANSPLANTATION (HD-ASCT) FOR CNS RELAPSE OF AGGRESSIVE LYMPHOMAS: A POTENTIALLY CURATIVE APPROACH?

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Background: CNS relapse of aggressive lymphoma has a poor prognosis with a median survival below six months. No standard of therapy has been defined. In this prospective multicenter phase II study a chemotherapy-only regimen including HD-ASCT is evaluated.

Methods: Adult (18-65 yrs.) immunocompetent patients with CNS relapse of aggressive lymphoma were eligible. Induction chemotherapy consisted of two cycles of high-dose methotrexate 4g/m^2 iv. (d1), ifosfamide 2g/m^2 iv. (d3-5) and ith. liposomal cytarabine 50mg (d6) and one cycle of high-dose cytarabine 3g/m^2 (d1-2), thiotepa 40mg/m^2 iv. (d2) and ith. liposomal cytarabine 50mg (d3). Then, patients without progression (PD) received carmustine 400mg/m^2 iv. (d -5), thiotepa 2x5mg/kg iv. (d -4 to -3) and etoposide 150mg/m^2 iv. (d -5 to -3) followed by ASCT.

Results: Thirty patients (median age 58 yrs.) were enrolled. Three patients had T-cell and 27 aggressive B-cell lymphoma. Median time to CNS relapse was 8.5 (3-80) mo. and was intracerebral in 24 and meningeal in 13 (combined in seven) patients; six had concomitant systemic lymphoma. Pretreatment was CHOP-like in 29 patients, including rituximab in 26. CNS disease responded to induction therapy in 22 (73%) patients (CR=10, PR=12); two had stable disease, four PD, and two were not evaluable for response. HD-ASCT was thus far performed in 23 patients; CNS response was 70%: CR=11, PD=5, and not yet evaluated =7. Systemic lymphoma responded in three evaluable patients: CR=2 and PR=1. Grade ≥3° toxicities included leucopenia (47%) and infection (20%); and - following HD-ASCT - mucositis (33%) and infection (61%). One patient died due to septic diverticulitis and one developed persisting fecal incontinence 4°. After a median follow up of 12.6 mo. the 1-year progression free survival was 60%.

Conclusions: This is the first prospective evaluation of HD-ASCT in this setting. The protocol used is highly active with tolerable toxicity. A prolonged follow up will determine its curative potential.

259 AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) IMPROVES SURVIVAL IN PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA (PCNSL)

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Background: Primary central nervous system lymphoma (PCNSL) is a rare extra-nodal non-Hodgkin lymphoma. Outcomes for PCNSL are poor and the standard of care for treatment remains unclear due to a lack of randomized studies. However, recent studies suggest that intensive chemotherapy with autologous stem cell transplantation (ASCT) is effective as salvage therapy and provides encouraging results as a part of primary therapy. In Alberta, PCNSL is treated exclusively in 2 centres; Centre B adopted ASCT for PCNSL only recently while Centre A has incorporated ASCT as a part of primary therapy or at relapse for > 10 years. Thus, patients were 'geographically randomised' to receive an ASCT-based therapy or not. We were thus able to compare the outcomes for patients treated with a strategy including ASCT versus a radiotherapy (RT)-based treatment.

Methodology: We performed a retrospective analysis of the outcomes of all patients diagnosed with PCNSL in Alberta from 1998-2008 to determine the 'real world' outcomes for this disease. We compared outcomes for patients treated at either Centre and for those who received ASCT or not. Cases of PCNSL were obtained from the Alberta Cancer Board Cancer Registry. Charts were manually reviewed and data extracted on clinical characteristics, treatment, response, toxicities, relapse and survival.

Results: was obtained for 95 patients with pathology-confirmed PCNSL of diffuse large B cell lymphoma (DLBCL)-type. The majority of patients (55%) were over age 60, had poor performance status (defined as ECOG ≥ 2 or KPS < 70) (70%) and had deep brain involvement (59%). The median age at diagnosis was 61 years. Elevation of LDH was uncommon (24%). Only 27 patients (28%) had a documented assessment of CSF protein level at diagnosis with 15 of these (56%) showing an elevated level. Two additional cases with non-DLBCL pathology were excluded from analysis (2 cases with epidural follicular lymphoma and 1 case of marginal zone lymphoma). Eight additional patients were diagnosed with PCNSL by radiology, without pathological confirmation. These patients had a median age of 80 and were uniformly palliated without chemotherapy or RT and were excluded from evaluation. The median follow-up for treated patients was 88 months. At Centre A, patients <70yrs without major organ dysfunction were offered ASCT if they did not achieve a CR with HDM or later relapsed. At centre B, patients were typically treated with WBRT and only 1 patient had ASCT as primary therapy and 1 patient underwent ASCT for relapsed disease. All but 3 ASCTs were performed following thiotepa, busulfan and cyclophosphamide (TBC) conditioning. Long-term event-free survival post-ASCT was seen in 11 of 18 patients transplanted in first partial remission, 1 of 3 patients transplanted for primary refractory/progressive disease, and 5 of 6 patients transplanted for relapsed disease. Three patients died early of transplant-related mortality (TRM). By univariate analysis, factors positively affecting OS included: treatment in Centre A (p=0.008), age ≤ 60 years (p=0.001), good performance status (ECOG 0-1) (p=0.014), treatment with HDM (p<0.001), treatment with ARA-C (p<0.001), CR/CRu as response to treatment (p<0.001), primary treatment with ASCT (p=0.01) and treatment at any time with TBC-ASCT (p<0.001). The 5 yr OS for patients with PCNSL who received an ASCT (at any time) was 66%, comparing favourably to historical reports. For those aged ≤ 65 (characteristics in Table 1), patients who received an ASCT at any time had a significantly improved survival (5 yr OS 70%) compared to those who did not (5 yr OS 20%) (p=0.009).

Conclusion: ASCT with TBC conditioning is an effective therapy for PCNSL both as a part of primary therapy and for relapsed disease. However, TBC/ASCT is associated with high TRM so efforts should be made to optimize ASCT conditioning to reduce toxicity and make this effective treatment available to more PCNSL patients.

Clinical characteristics of HIV- patients ≤ 65 years treated in Alberta 1998-2008 Table 1.

Characteristic	Ever TBC-ASCT	Never TBC-ASCT
Number of patients	23	27
Median age (range)	55 (30-65)	56 (36-65)
Age > 50 (%)	13 (56)	19 (70)
ECOG ≥ 2 (%) or KPS<70	18 (78)	17 (63)
Deep brain involvement (%)*	14 (61)	14 (54)
Elevated LDH (%)*	5 (25)	3 (14)
Immune suppressed (%)	1 (4)	2 (7)
Prior RT treatment (%)	3 (13)	15 (55)
Prior HDM treatment (%)	23 (100)	15 (55)
Alive & well (%)	15 (65)	9 (33)
Death due to PCNSL (%)	3 (13)	13 (48)
Non-PCNSL death (%)	5 (22)	5 (18)

% calculation excludes patients for whom the information was not available