Session 7: aggressive lymphoma

071 MYC + AGGRESSIVE-B-CELL LYMPHOMAS: NOVEL THERAPY OF UNTREATED BURKITT LYMPHOMA (BL) AND MYC + DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) WITH DA-EPOCH-R

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Background: MYC translocations are associated with a high proliferation and poor outcome in B-cell lymphomas treated with CHOP-based regimens. In BL with MYC translocations, multidrug intensive chemotherapy is effective but associated with significant toxicity and mortality. Recent reports indicate that 10% of DLBCLs also have MYC translocations.

Methods: We hypothesized that DA-EPOCH-R may be effective in MYC+ aggressive lymphomas based on its efficacy in highly proliferative DLBCL. We compared it with conventional first-line treatment of DA-EPOCH-R with or without high-dose therapy (HDT) in a randomized phase III trial, with a 2x2 factorial design, to compare two R-dose-dense chemotherapies, RCHOP14 (RC14) with RCHOP.

Results: Characteristics of 29 BL are median age 35 (16-88); male sex 22 (76%); and 12 (41%) cases were HIV negative. At a median follow-up of 48 months, the EFS of MYC+ DLBCL is 83% and 76%, respectively (P=0.46; Exact two-tailed log-rank). Notable toxicities were tumor lysis syndrome (1 pt) and fever/neutropenia in 16% of cycles. Dexamethasone + Rituximab (R). We wanted to improve outcome for such pts by escalating dose and intensity of RCHOP14. A more aggressive dose-dense chemotherapy does not seem to play a significant role. So far, this advantage in PFS does not translate in overall survival differences. A more aggressive dose-dense chemotherapy does not seem to play a significant role. So far, this advantage in PFS does not translate in overall survival differences.

Conclusions: This randomized trial showed that HDT, as first line treatment in young high-risk DLBCL, significantly reduced the relapse rate in comparison to standard RCHOP14. A more aggressive dose-dense chemotherapy does not seem to play a significant role. So far, this advantage in PFS does not translate in overall survival differences. A more aggressive dose-dense chemotherapy does not seem to play a significant role. So far, this advantage in PFS does not translate in overall survival differences.
the R-CHOEP-14 arm (p = 0.348). The overall response rate was 77.9 % (CR/CrR 75.1%, PR 2.8%). Three-year-progression-free survival (PFS) was 73.7% for pts treated with 8 x CHOEP-14 plus R compared to 69.8% in pts given 4 x MegaCHOEP plus 6 x R (p = 0.475). Three-year overall survival (OS) was 84.6% in pts treated with 8 x CHOEP-14 as compared to 77.0% in pts given 4 x MegaCHOEP plus 6 x R (p = 0.081). OS was significantly better for pts with adILP 2 who received conventional chemotherapy plus R (p = 0.013) while survival curves for pts with adILP 3 were superimposable.

Conclusions: Conventional chemotherapy 8 x CHOEP-14 in remission in excellent PFS (73.7 %) and OS (84.6%) representing the best results ever reported for young, high-risk pts with aggressive B-cell lymphoma. Conventional therapy was significantly better than HDT/ASCT in pts with adILP 2; no significant differences were seen overall and in pts with adILP 3. In the Rituximab-era, HDT/ASCT should no longer be considered standard first-line therapy for young, high-risk pts with aggressive B-cell lymphoma.

074 RANDOMIZED PHASE II STUDY OF R-CHOP PLUS ENZASTAURIN VERSUS R-CHOP IN THE FIRST-LINE TREATMENT OF PATIENTS WITH INTERMEDIATE AND HIGH-RISK DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) – PRELIMINARY ANALYSIS

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Background: The combination of rituximab plus CHOP chemotherapy (R-CHOP) is widely used as standard of care for DLBCL; however, long-term survival is low in patients (pts) with high International Prognostic Index (IPI) risk scores. Enzastaurin (ENZ) targets protein kinase C-β (PKCβ), an enzyme correlated with poor pt outcomes in DLBCL. In this trial, we compared the results of first-line treatment with R-CHOEP + ENZ to standard R-CHOP.

Material and Methods: DLBCL pts were required to have intermediate or high-risk IPI scores (2-5). Pts were randomized (3:2 ratio) to receive six 21-day cycles of either R-CHOP + ENZ therapy (Arm A) or R-CHOP alone (Arm B). After 6 cycles, responders in Arm A could continue single agent ENZ. An 1125 mg oral loading dose of ENZ was given on Day 2 followed by 500 mg ENZ daily. Response was evaluated (IWG criteria, 1999) q8 weeks. The primary endpoint was progression-free survival (PFS). Randomization of 100 pts allowed detection of an improvement in the PFS at 2 years from 63% (R-CHOP) to 80% with R-CHOP + ENZ (80% power, 1-sided alpha 0.2). This preliminary analysis was performed after all pts had completed R-CHOP chemotherapy, and had been followed for at least 1 year.

Results: Pt characteristics were comparable in Arm A (N=57) and Arm B (N=43). A total of 65 pts (65%) had either high-intermediate (44%) or high (21%) IPI risk scores. The median PFS has not yet been reached; however, the 1-year PFS rate for Arm A was 71% (CI 0.58, 0.84) and Arm B 52% (CI 0.35, 0.69). Overall response rates for Arms A and B were 80.4% and 83.3%, respectively; complete response rates were 35.7% and 26.2%. Most frequent grade 3/4 adverse events were neutropenia (51.4% v 51.1%) and thrombocytopenia (vs 13.9%) (Arm A vs B). In Arm A 2.3% and in Arm B 9.3% of pts had grade 3/4 infection-related complications. In Arm A 4 pts died (sepsis 2, pulmonary embolism 1, and ARDS 1) and in Arm B 3 pts (sepsis 2, pneumonia 1).

Conclusions: This preliminary analysis suggests an improvement in PFS and complete response rate for pts with intermediate or high-risk DLBCL treated with R-CHOP + ENZ compared to standard R-CHOP, with comparable toxicity profiles. Final analysis will be conducted after 2-year followup.

075 SALVAGE REGIMEN WITH AUTOLOGOUS STEM CELL TRANSPANTATION WITH OR WITHOUT RITUXIMAB MAINTENANCE FOR RELAPSED DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL): CORAL FINAL REPORT

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Background: Chemotherapy followed by autologous stem cell transplantation (ASCT) is the standard treatment for relapsed DLBCL. No study has compared salvage therapies and evaluated maintenance post ASCT.

Methods: DLBCL CD 20+ in first relapse or pts refractory after first therapy were randomized between R ICE (rituximab, ifosfamide, etoposide, carboplatinum) or R DHAP (rituximab, dexamethasone, cyclosphamide, cisplatinum). Responding patients received BEAM and ASCT then randomized between observation or maintenance with rituximab every 2 m for 1 yr (Gisselbrecht J Clin Oncol; 2010).

Results: Analysis was made on 477 pts (R ICE: 243 pts; R DHAP: 234 pts): 255 relapsed & 122 early relapsers; 106 pts had prior rituximab; secondary(s) IPI 0-1: 281 pts; IPI 2-3:181 pts. There was no difference in response rate between R ICE 63.6% and R DHAP 64.3%. There was no difference between R ICE and R DHAP at 4 yrs for EFS (26% vs 37% p=0.02) and OS (43% vs 51%, p=0.3). Factors affecting 4 yrs EFS, PFS and OS were: prior treatment with rituximab; early relapse< 12 m: IPI 2-3. ASCT was performed in 255 pts and 242 randomized for maintenance: 122 pts rituximab (R), 120 pts observation (O). Distribution between R/O arms were respectively: median age 54 /53 yrs, Male 76/83%; female 46/57%; secondary IPI 0-1: 84/81%; sIPI 2-3: 36/36, 89/76 relapses >12m., 33/41 refractory/early relapses. Median follow up was 44 m with 111 events. 4 yrs PFS was 52.8 % (CI 46-59) with 63% (CI 56-69) OS. There was no difference in EFS, PFS and OS between R and O arms. In multivariate analysis, sIPI2-3 significantly affected EFS, PFS and OS (p=0.0004). Women (83pts) had a better 4 yrs EFS 63% than male (159pts) 37% (p=0.01). The difference was only in the R arm (p=0.004). Gender was an independent prognostic factor in the R arm. Toxicity was mild with 12% SAE versus 4% for R /O respectively.

Conclusions: There was no difference between R ICE and R DHAP and between post ASCT maintenance with R or O. Women did significantly better after ASCT with rituximab. Early relapses to upfront rituximab-based chemotherapy have a poor prognosis.