092 CORRELATION BETWEEN EPSTEIN-BARR VIRUS (EBV) RNA EXPRESSION AND VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) EXPRESSION IN DIFFERENT SUBTYPES OF PERIPHERAL T-CELL LYMPHOMAS (PTCL) AND PROGNOSTIC IMPLICATIONS

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Background: EBV is known to be associated with various lymphoid malignancies. An up-regulation of EBV by EBV has been suggested. The aim of this study was to investigate the correlation between the expression of EBER and angiogenic molecules in PTCL and to examine their possible prognostic impact.

Material and methods: Tissue sections from 62 PTCL (36 PTCL-unspecified (PTCL-u), 1 NK/T nasal type, 7 angioimmunoblastic (AIL), 8 anaplastic large cell (ALCL)) were analysed. Expression of EBER1 and VEGF mRNA were detected by in situ hybridization (ISH). The expression of LMP-1 protein was examined by immunohistochemistry (IH). In 44 cases, the expressions of VEGF, VEGF-C, Flt-1, KDR and Flk-2 were also estimated by IH.

Results: EBER expression was detected in 37% of all PTCL cases (PTCL-u 38%, AIL 85%, ALC 16%). Strong EBER positivity correlated to higher VEGF mRNA expression, both in the entire cohort analysed (p=0.02) and separately in PTCL-u (p=0.02). High EBER expression correlated to nuclear Flt-4 expression (p=0.01). Cases showing diffuse expression of VEGF mRNA had significantly poorer event-free (p=0.02) and overall (p=0.04) survival than cases with focal or no expression. Higher EBER expression was correlated with higher IPI (p=0.01), but had no impact on survival when all PTCL cases were analysed together. Analysed separately for PTCL-u, a high EBER expression predicted a poorer event-free survival (p=0.02) and tended to be associated with adverse impact on overall survival (p=0.08).

Conclusions: EBV RNA was detected in 37% of all PTCL cases analysed. Strong EBER expression significantly correlated to higher VEGF mRNA and nuclear Flt-4 expression, suggesting that EBER may up-regulate angiogenic pathways in lymphoma cells. Diffuse VEGF expression was associated with an adverse impact on outcome. In PTCL-u, EBER predicted poorer outcome.

093 A NEW PROGNOSTIC MODEL FOR PERIPHERAL T/NK-CELL LYMPHOMAS (PTCLS) FROM PROSPECTIVE MULTICENTER CLINICAL TRIALS

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Background: PTCLs are known to show a worse survival than B-cell lymphomas. There are also reports of better survival in group 1, 2 and 3, 4 factors. This novel prognostic index for PTCLs was able to efficiently identify 3 groups of pts with different outcomes (p=0.0001). For the 49 pts in group 1, the 2-year and 5-year survival rates were 75.5% and 61.2%, respectively; for the 66 pts in group 2, 56.1% and 42.3%; and for the 16 pts group 3, 31.3% and 12.5%.

Conclusions: Our study indicates that PTCL pathological subtypes are important prognostic factors in PTCL. A new prognostic model for PTCLs warrants further validation studies. (Supported by 2S-1, 5S-1, 8S-1, 11S-1, 4, 14S-1, 4, 17S-1, 5)

094 T-CELL LYMPHOMAS IN STUDIES OF THE GERMAN HIGH-GRADE NHL STUDY GROUP (DSHNHL)

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From 1993 to 2006 331 patients (pts) with mature T cell lymphoma were treated on DSHNHL protocols NHL-B1 (98 pts), NHL-B2 (41 pts), highCHOEP phase III/III (74 pts), MegaCHOEP phase II/III (59 pts), and RICOVER60 (59 pts). 207 pts were male, the median age at study entry was 50 years (yrs). LDH was elevated in 34% of pts, 48% had stage III/IV disease, ECOG performance status was >1 in 166 and more than one extranodal involvement was present in 18% of pts resulting in IPI low in 54%, lower-intermediate in 24%, high-intermediate in 19%, and high in 9% of pts. Median observation time for all pts was 3.6 yrs. OS and EFS were 65% and 51%, respectively, at 3 yrs. Significant differences in OS were found according to IPI scores. In univariate analyses OS and EFS were significantly influenced by the presence / absence of any IPI factor. In a multiple Cox model the IPI factors except advanced stage (III/IV) remained significant. Interestingly, younger pts (<60 yrs) with good-risk disease (LDH <N) showed significantly better 5-yrs EFS (71 vs 30%) when compared with ETO was added to CHOP-14 or -21 (p=0.010). Elderly pts (>60 yrs) did not benefit from addition of ETO; however, there was a trend for better EFS in the elderly if CHOP-14 instead of CHOP-21 was used (p=0.069). Furthermore, in the RICOVER study pts >60 yrs did not show a benefit if 6 instead of 4 courses of CHOP-14 were administered. Overall, OS and EFS for pts with mature T cell lymphoma treated on DSHNHL studies are encouraging. Findings reported earlier for pts with aggressive B-cell lymphomas were also present in pts with T cell lymphoma: 1. CHOEP resulted in superior EFS over CHOP in younger but not in elderly pts. 2. CHOP-14 was superior to CHOP-21 in the elderly, and 3. the administration of 2 further courses of CHOP-14 did not improve outcome over 6 courses. Also, the IPI proved a robust tool to predict OS and EFS in pts with mature T cell lymphoma.
PTCL ↔ PHASE II STUDY OF DENILEUKIN DIFTITOX WITH CHOP IN TCL pts who will be cured by ASCT and to select pts who will need other approaches. 

Denileukin diftitox (Dd) is a recombinant fusion toxin which targets the interleukin-2 receptor and has demonstrated a 50% response rate in patients with relapsed/refractory PTCL. Because of poor overall outcomes for patients with PTCLu and other aggressive T-cell lymphoma subtypes, we initiated a Phase II study to evaluate the safety and efficacy of the combination of Dd with CHOP as first line therapy in patients with PTCL. Dd was administered at a dose of 18 ug/kg/day for days 1, 2 and CHOP on day 3 every 21 days for 6 cycles. All patients received G-CSF support. Of 47 enrolled patients, the median age was 52. Twenty-two patients had PTCLu, 12 had angioimmunoblastic T-cell lymphoma, 6 had ALCCL, and 7 had other subtypes. Thirty-seven patients were evaluable for response. The overall response rate was 89% with 29/37 (78%) CR, 4/37 (11%) PR, 3/37 (8%) SD. Eleven of 37 responders (30%) have progressed, and the median response duration has not been reached. The median PFS is 17 mo. December with 3-7 controls with other lymphomas in the breast, matched on year of diagnosis (no proven lymphoma, primary cutaneous lymphoma, relapse in the breast diagnosed between 1990 and 2006 was performed in the Netherlands. Eleven patients with ALCCL in the breast were retrieved for whom complete clinical and pathological information were collected. Subsequently, a matched case-control study was performed with 3-7 controls with other lymphomas in the breast, matched on year and age of diagnosis. Pathological and clinical information was obtained with specific emphasis on the presence of a breast prosthesis. Logistic regression analysis was performed to estimate the relative risk of ALCCL associated with breast prosthesis. Results: 11 patients with ALCCL of the breast were identified, diagnosed between 1994 and 2006 with a median age of 40 years (range 25-68 years). Of these, in 4 patients bilateral silicone breast prosthesis were placed 3, 4, 13 and 22 years prior to diagnosis all for cosmetic reasons. Similar cases have been reported in the literature. An increased risk of ALCCL in patients with breast prosthesis has been speculated but no studies have been conducted so far. Methods: A comprehensive search (PALGA) for all patients with lymphoma in the breast diagnosed between 1990 and 2006 was performed in the Netherlands. Eleven patients with ALCCL in the breast were retrieved for whom complete clinical and pathological information were collected. Subsequently, a matched case-control study was performed with 3-7 controls with other lymphomas in the breast, matched on year and age of diagnosis. Pathological and clinical information was obtained with specific emphasis on the presence of a breast prosthesis. Logistic regression analysis was performed to estimate the relative risk of ALCCL associated with breast prosthesis. Background: Recently, we identified two patients with anaplastic large T-cell lymphoma (ALCL, ALK-) in the fibrous capsule of silicone breast prosthesis, placed for cosmetic reasons. Similar cases have been reported in the literature. An increased risk for the development of ALCL associated with breast prosthesis of 20 (95% CI: 1.9-207). 

Conclusion: This study suggests a strongly elevated risk for developing an ALCCL in the breast in the context of silicone breast protheses placed for cosmetic reasons.