**151 IS THE NATURAL HISTORY OF HODGKIN LYMPHOMA (HL) CHANGING?**

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**Introduction:** Age specific incidence (ASI, here expressed as cases per 100,000 population) for HL characteristically shows a bimodal distribution with a third decade peak, fifth decade trough and gradual rise in numbers with increasing age. This pattern is similar for both sexes, with relative excess of males at all ages.

**Methods:** We conducted consecutive audits in the South West of England, encompassing 22 hospitals, for the years 1993 (96 cases), 1999 (93) and 2005 (148), to examine the patient diagnostic and treatment pathways and long term outcomes. Unselected cohorts included all HL known to the diagnosing hospital. None of the participating units varied between the three audits and an accurate estimate of the underlying population and ASI of HL was not possible from the data obtained.

**Results:** Complete SWP/HL cancer registry data for the same periods were therefore examined.

**Conclusions:** 1) Regional audit uncovered a possible change in the recognised bimodal distribution. However, the 2005 cohort showed a similar shifted age distribution for males in the fifth decade: 1993: 2.47 (1.06-4.86) 1999: 2.21 (0.89-4.56) 2005: 6.38 (3.95-9.76). This unexplained change was not seen for females and the relative ASI remained stable for both sexes for other age except for the 5th and 9th decades where increases were likely to be due to case ascertainment.

**152 U-HO1, A NEW CEL LINE DERIVED FROM A PRIMARY REFRACTORY CLASSICAL HODGKIN LYMPHOMA**

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**Introduction:** Although Hodgkin lymphoma (HL) is not a rare disease and the occurrence of HL in young patients point to a genetically determined risk factor, its molecular oncogenesis is largely unknown and less than 10 HL cell lines exist worldwide. Here we describe a novel permanent human HL cell line, U-HO1, derived from the end stage of refractory nodular sclerosing classical HL of a male patient.

**Results:** Since its establishment in 2005, U-HO1 has maintained stable characteristics in vitro and has a doubling time of about 4 days under standard culture conditions. U-HO1 forms typical Reed-Sternberg cells in suspension, is EBV negative, lacks HLA-DR expression and activity of the common cytokine-receptor type II (IL-2, IL-13, IL-12, IL-4), and has a doubling time of about 4 days under standard culture conditions. U-HO1 revealed a hyperdiploid karyotype with multiple clonal abnormalities. Most significant is an elongated chromosome 2, der(2)(q21;q14) by FISH analysis. On a cellular level, U-HO1 is highly expressing the CD40 ligand (CD154), which plays a role in the activation of CD4+ T cells. Furthermore, U-HO1 expresses CD20, CD45, CD79a and MHC class II antigens, and is negative for the expression of CD5, CD10, and BCL-2. U-HO1 also shows high expression of the late activation antigens CD30 and MUM1 and has a normal karyotype.

**Conclusion:** U-HO1 is a novel cell line derived from a primary refractory classical HL which may become a valuable tool for research in HL.

**153 DEPLETION OF GLUTATHIONE ENHANCES ARSENIC TRIOXIDE (AS2O3)-INDUCED APOPTOSIS THROUGH MITOGEN ACTIVATED PROTEIN KINASE (MAPK) PATHWAYS IN HODGKIN LYMPHOMA (HL) AND NON-HODGKIN LYMPHOMA (NHL) CELLS**

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**Introduction:** Although Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) and have therapeutic implications. Inhibitors of MEK1/2 and JNK enhanced As2O3 induced apoptosis in Ramos. Immunoblot analyses were performed for bcl-2, PARP, cleaved caspases and MAPK pathways (ERK, JNK, and p38).

**Results:** As2O3 alone resulted in dose and time dependent apoptosis in all cell lines (HL and NHL) with >75% Annexin/PI at 48-72 hours. In Ramos and L428 cells, a combination of As2O3 (2μM) and BSO 100μM was synergistic resulting in >80% Annexin/PI, while either agent alone resulted in <15% apoptosis (p<0.001). A 4-fold increase in ROS was seen in all cell lines with As2O3/BSO. Both ROS and apoptosis induced by As2O3/BSO were reversible with the anti-oxidant N-acetylcysteine (NAC) (10μM). Furthermore, As2O3 induced PARP and caspase-3 cleavage in all NHL cell lines, but not L428. In Ramos, Z-VAD-FMK and Z-IETD-FMK blocked As2O3 induced apoptosis (suggesting a caspase-dependent mechanism), but had no effect on As2O3/BSO-induced cell death (caspase-independent). We found up-regulation of p-p38 in Ramos cells, while in L428, p-ERK was activated with As2O3/BSO and As2O3. Inhibition of MEK1/2 and JNK enhanced As2O3 induced apoptosis.

**Conclusion:** As2O3 alone induced dose- and time-dependent apoptosis in HL and NHL cells, which was significantly enhanced with the addition of BSO. Furthermore, As2O3/BSO-related apoptosis was ROS dependent. As2O3 alone resulted in caspase-dependent apoptosis, while addition of BSO resulted in caspase-independent apoptosis. In Ramos, Z-VAD-FMK and Z-IETD-FMK blocked As2O3 induced cell death (caspase-independent). We found up-regulation of p-p38 in Ramos cells, while in L428, p-ERK was activated with As2O3/BSO and As2O3. Inhibitors of MEK1/2 and JNK enhanced As2O3-induced apoptosis in Ramos.

**154 ABRUPT EXPRESSION OF THE TH2 CYTOKINE IL-21 IN HODGKIN LYMPHOMA CELLS REGULATES STAT3 SIGNALING AND ATTRACTS TREG CELLS VIA REGULATION OF MIP-3α**

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**Introduction:** The malignant Hodgkin-Reed-Sternberg (HRS) cells of Hodgkin lymphoma (HL) are derived from mature B cells, but have lost the B cell-specific gene expression pattern. Consequences of such a lineage infidelity for lymphoma pathogenesis are currently not defined. Here, we report on HRS cells an aberrant expression and activity of the common cytokine-receptor γ-chain (cyt) cytokine IL-21, which is usually restricted to a subset of CD4+ T cells.

**Material and Methods:** Experiments were performed using a panel of HRS and non-Hodgkin cell lines. The analysis of IL-21 and MIP-3α expression and activity was performed by use of RT-PCR, Western blot and FACS analysis, ELISA, treatment with anti-IL-21, specific inhibition of IL-21 signaling, and migration assays with freshly isolated PMNC. Apoptosis was analyzed by Annexin/V FITC cytometry staining. Primary HL cases were analyzed for expression of MIP-3α and IL-21 by IHC. Results: IL-21 activates STAT3 in HRS cells, up-regulates STAT3 target genes, and protects HRS cells from CD95 death receptor-induced apoptosis. Furthermore, IL-21 is involved in up-regulation of the CC chemokine MIP-3α in HRS cells which in turn attracts regulatory T cells towards HRS cells. IHC analyses confirmed expression of IL-21 and MIP-3α in HRS cells in 9 out of 10 HL cases analyzed, independent of the EBV status.
156 COMBINATION OF GENE PROFILING AND TISSUE MICROARRAYS IDENTIFIES THE B-CELL/PLASMACYTOID DENDRITIC CELL–SPECIFIC GENE BCL11A AS A ROUTINE MARKER OF FAVOURABLE OUTCOME IN CLASSICAL HODGKIN LYMPHOMA

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Background: After treatment for classical Hodgkin lymphoma (cHL), about 40% of patients present either refractory disease or relapse. Identification of patients who would require more intensive therapy is thus a crucial challenge.

Methods: A training set of 63 cHL frozen tissue samples was profiled using Affymetrix microarrays. A validation set of paraffin tissue samples from 154 cHL patients (median follow-up of 75.7 months) was analysed using immunohistochemistry (IHC) on tissue microarrays.

Results: Using a supervised analysis, the signature of EBV+ vs EBV- HL tissues was enriched in genes characteristic of Th1 and antiviral responses including IFNG. 38 genes were significantly overexpressed in HL patients with complete remission, when compared to those with refractory disease or relapse. They were involved in the function of B-cells and plasmacytoid dendritic cells (pDCs), like BCL11A. IHC validation using both univariate and multivariate Cox models confirmed that high expression of BCL11A was associated with longer event-free survival (p < 0.01). Univariate Cox model showed a significant correlation between high expression of BCL11A and increased event-free survival (p < 0.01). High expression of BCL11A was predictive of favourable outcome in cHL, independently of EBV status.

Conclusions: BCL11A as a powerful routine IHC prognosis marker might help to select cHL patients who would benefit from reduced therapy to avoid late toxicity. This also suggests that innate immunity, including pDCs, play an important role in the defence against cHL tumor cells. Thus, stimulation of pDC activity and intra-tumoral Th1 responses against EBV may be a basis for novel treatment strategies.

157 MECHANISMS OF DEPSIPETIDE INDUCED CELL DEADTH IN REED-Sternberg CELLS

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Background: It was speculated that simultaneous inhibition of multiple signalling pathways might be a promising strategy to target HL. In the present study we tested the effect of histone deacetylase (HDAC) inhibition using depsipeptide (trichostatin A) in cell lines in vitro.

Material and Methods: Molecular mechanisms of toxicity were analyzed in HL cell lines (L1236, L218, L941, L540Cy) using viability and apoptosis assays with z-vad-fmk as a pan-caspase inhibitor. In addition, whole genome RNA expression analysis (Affymetrix Array 133 Plus2.0) and functional NFκB binding assays (TransAM) were performed.

Results: It is shown that depsipeptide is effective at submicromolar concentrations in all cell lines studied. It acts mainly by apoptosis induction as shown by caspase activity, biochemical assays and FACS, and upregulation of p21, and cell cycle inhibition in G2/M. It is also shown that HDAC induces upregulation of RelA/p65 binding activity.

Conclusion: Depsipeptide induced protein acetylation results in transcriptional changes of a large number of pathogenetically relevant genes, especially of apoptosis and cell-cycle related genes. It induced toxicity in all cell lines studied despite the striking finding of increased RelA/p65 binding activity in depsipeptide treated cells. Our preclinical data suggest that HDAC inhibition using depsipeptide might be a promising approach for the treatment of patients with HL.

158 SHIELD - STUDY OF Hodgkin LYMPHOMA IN THE ELDERLY/ Lymphoma Data Base: Progress Report

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Introduction: Hodgkin lymphoma (HL) is a curable disease but outcome in patients >60 years has not improved. The SHIELD programme offers a phase II interventional study (VEPEMB: vinblastine, etoposide, prednisolone, procarbazine, endoxan, mitoxantrone, bleomycin) and a registration element for patients ineligible because of frailty/palliative approach or use of an alternative regimen.

Results: At January 2008 a total of 153 patients had been enrolled in the programme. 64/153 VEPEMB patients; age range 60-85 years, median age 72 years, Stage I and II 28/64 patients (receiving VEPEMB x 3 or x 4), 3/64 stage III and IV patients (receiving VEPEMB x 6 or x 8) and 1/64 patients not known. 30/64 completed full course of treatment, 15/64 required major dose reduction or discontinued therapy and 19/64 patients data pending. Histological types: 26/64 mixed cellularity, 27/64 nodular sclerosis; 7/64 unclassified; 4/64 lymphocyte rich. There were no treatment related deaths in the VEPEMB study but grade III/IV haematological toxicity was encountered in later courses requiring use of routine G-CSF. Deaths on VEPEMB treated patients were 3/64 as a result of HL and 5/64 deaths not related to disease or treatment.

Discussion: This on-line study programme has already prospectively accrued the largest number of HD elderly patients worldwide, and is set to double the number in a two year period. Such a study approach is applicable to other rare ‘orphan’ areas of lymphoma research. Web site www.shieldstudy.co.uk

159 IS ROUTINE BONE MARROW BIOPSY NECESSARY IN STAGING PATIENTS WITH Hodgkin DISEASE IN THE PET ERA?

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Background: The use of positron emission tomography (PET) scans in Hodgkin’s lymphoma (HL) staging significantly reduce the need for bone marrow (BM) biopsy. However, BM biopsy remains a standard of care in some centers.

Methods: We retrospectively reviewed 264 consecutive presentations with newly diagnosed HL and who had both PET/CT and BMB before start of treatment.

Results: 4/48 patients had lymphomatous involvement on BM. All 4 those patients were also positive on PET/CT scan. In 9 additional patients, PET/CT scan showed multiple foci suggestive of bone/bone marrow involvement. Further confirmation of these lesions was obtained by BM in 3 patients and on pretreatment CT in 1. BM findings on PET/CT led to upstaging of 6 patients with initial stage II or III; 3 others were already stage IV.

Conclusion: PET/CT appears better than BM to detect bone/bone marrow involvement. We therefore conclude that, in patient with pre-treatment negative PET/CT, BM is probably not justified.

160 RISK ADAPTED BEACOPP BASED ON EARLY INTERIM SPECTROGRAPHY CAN BE USED FOR REDUCTION OF CUMULATIVE DOSE OF CHEMOTHERAPY AND PRESERVATION OF FERTILITY IN PATIENTS WITH STANDARD AND HIGH RISK HODGKIN LYMPHOMA (HD)

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This prospective study evaluated outcome of HD pts whose therapy was tailored based on results of scans performed after 1 or 2 cycles of chemotherapy, thus reducing dose for early responders and maximizing the dose for slow responders. The study was started in 1999 for pts with HD aged 18-65 yrs. Eligibility criteria were unfavorable stages I-II and stage III or IV. Disease was defined according to the International Prognostic Score (IPS). Standard risk pts were treated with 2 cycles of standard BEACOPP (SB) and those with IPS ≥ 3 got 2 cycles of escalated BEACOPP (EB). Baseline Ga5+ or hybrid PET/CT scan was done at diagnosis and after the 1st or 2nd cycle for SB and 66 pts, respectively. If early interim scan remained positive, additional 4 cycles of EB were used; otherwise SB was given. The data were previously reported (Blood, ASH 2003); herein is an update with longer follow-up and 16 added patients.124 pts aged 18-65 yrs (median 31) are reported: CR rate was 97%, 5-y event-free (EFS) and overall survivals (OS) were 87% and 92%, respectively at a median follow-up of 55 m (5-95). 5-y EFS and OS were similar for standard and high risk pts. HD progressed in 3/12 pts with interim positive PET/CT versus 1/34 with negative PET (p=0.02). Negative predictive values of early normal PET and Ga5+ scans are 98% and 84%, respectively, p<0.03. One pt developed secondary leukemia after relapse and high-dose chemotherapy. One pt died from an unrelated cause. 37 females < 40 years old were assessed for fertility status: 14 conceived during follow-up and delivered 12 healthy babies, 1 is currently pregnant and 2 terminated their pregnancy. 17 other patients had cyclic ovarian function, 83% kept their ovarian function. Conclusion: PET/CT was useful for making an early interim decision about chemotherapy dose on an individual basis. The results of 6 cycles of risk-adapted BEACOPP compare favorably with the reported data following 8 cycles of EB.

161 FDG-PET FOR ASSESSMENT OF EARLY THERAPY RESPONSE AFTER 4 CYCLES OF CHEMOTHERAPY IN ADVANCED STAGE HODGKIN LYMPHOMA

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Introduction: The aim of this study is to assess predictive value of PET after four cycles of BEACOPP therapy of advanced stage of HL treated within HD15 study of GHSG.

Material and methods: Total of 30 pts were evaluated. Median follow – up of living pts is 22 months and median age 29 years. One patient PET negative died due to acute toxicity of treatment.

Results: 36/50 pts had negative and 14/50 pts (28%) had positive PET after four cycles of BEACOPP (PET4): 13/14 had initially a large mediastinal mass, IPS 3 – 6 in 26 pts, 2 – 1 in 4 pts. After the completion of chemotherapy, nine patients had residual disease. This finding supports again well known observation that the large mediastinal mass is the high risk factor and requires intensive type of treatment. However, considering still low number of patients and short follow-up, any definite conclusion regarding the prognostic impact of this finding is pending. Supported by Grant MZ CR IGA NR 8033 – 6/2004.

162 10-YEAR RESULTS OF THE HD9 TRIAL OF THE GERMAN HODGKIN STUDY GROUP (GHSG) COMPARING BASELINE AND ESCALATED BEACOPP CHEMOTHERAPY FOR ADVANCED HODGKIN LYMPHOMA

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The HD9 trial compared two different doses (baseline and escalated) of the novel chemotherapy regimen BEACOPP in advanced Hodgkin lymphoma. The previous analysis with a median follow-up of 5 years showed improved tumor control and overall survival for BEACOPPescalated. The present 10 year analysis in March 2007 aimed to update and confirm these results and to monitor late effects. Patients aged 16-65 yrs with untreated advanced Hodgkin lymphoma (stage II/IIB and risk factors or stage III/IV) were randomized to (A) 4 double cycles COPP/ABVD, (B) 8 cycles BEACOPPbaseline, or (C) 8 cycles escalated BEACOPP (doxorubicin, cyclophosphamide and etoposide at 140%, 192% and 200% of standard doses, respectively). The chemotherapy was followed by irradiation of initial bulky and residual disease for all treatment arms. Accrual of at least 900 patients was planned so as to detect a 9-10% improvement in the primary endpoint, freedom from treatment failure (FFTF). 1196 of 1201 eligible, randomized patients were evaluable (261, 409 and 466 in arms A, B and C, respectively). The median follow-up times were 122, 111 and 107 months in arms A, B and C, respectively (29-32 months longer than in 2004). Corresponding 10-year FFTF rates were 64%, 70% and 82% respectively (p<0.0001). FFTF was significantly better in the escalated BEACOPP arm than in the BEACOPPbaseline arm (p<0.0001). 10-year overall survival rates were 75%, 80% and 86% respectively (p=0.0001). Overall survival was also significantly better in the BEACOPPescalated arm than in the BEACOPPbaseline arm (p=0.0001). The present 10 year analysis in March 2007 aimed to update and confirm these results and to monitor late effects. Patients aged 16-65 yrs with untreated advanced Hodgkin lymphoma (stage IIB/IIIA and risk factors or stage IIIB/IV) were randomized to (A) 4 double cycles COPP/ABVD, (B) 8 cycles escalated BEACOPP (doxorubicin, cyclophosphamide and etoposide at 140%, 192% and 200% of standard doses, respectively). The chemotherapy was followed by irradiation of initial bulky and residual disease for all treatment arms. Accrual of at least 900 patients was planned so as to detect a 9-10% improvement in the primary endpoint, freedom from treatment failure (FFTF). 1196 of 1201 eligible, randomized patients were evaluable (261, 409 and 466 in arms A, B and C, respectively). The median follow-up times were 122, 111 and 107 months in arms A, B and C, respectively (29-32 months longer than in 2004). Corresponding 10-year FFTF rates were 64%, 70% and 82% respectively (p<0.0001). FFTF was significantly better in the escalated BEACOPP arm than in the BEACOPPbaseline arm (p<0.0001). 10-year overall survival rates were 75%, 80% and 86% respectively (p=0.0001). Overall survival was also significantly better in the BEACOPPescalated arm than in the BEACOPPbaseline arm (p=0.0001).
pts, a 30-y-old man, with residual PET/lesions at the end of the 4th cycle, was considered a failure. Finally, 3637 (97%) pts were in CR at 21 days. Two pts (0.5%) had a biopsy-proven relapse (<1:2:mo): a 29-y-old girl (CS IVEB) and a 33-y-old man (CS IVEA). A 60-y-old man (CS IVEB) died of pneumonia 1-mo after the end of the last cycle. All the other pts were alive and free of disease. With a median follow-up of 20 (range 4-41) and 22 (6-43) months, the DFS and OS were 92% and 97% respectively: no significant differences were registered among stage-subsets. Hematologic toxicity was moderate and self-limiting, with grade 3 or 4 neutropenia and anemia occurring in less than 20% of courses. A limited number of G3-G4 events determined the need for intervention or hospitalisation. 

**Conclusions:** dd-di-ABVD is feasible, well tolerated and highly active in newly diagnosed patients with HR HL.

### 165 HIGH-DOSE SEQUENTIAL CHEMOTHERAPY (HDS) FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) IN RELAPSING/REFRACTORY HODGKIN LYMPHOMA (HL): LONG-TERM RESULTS

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**Introduction:** Starting from January 1986 235 patients (pts) were enrolled in a multicenter clinical trial to explore the role of HDS followed by ASCT in refractory or relapsed HL.

**Patients and methods:** The mean age was 32.4 (11-61), limited (II) or advanced stage (II IV) in 104 and 131 pts, respectively. The first-line chemotherapy consisted in ABVD in 126 pts., hybrid/alternating MOPP/ABVD in 57, or other in 52. Two or more lines of chemotherapy were given in 22 patients. HDS plus ASCT was given for resistant or relapsing disease in 63 and 172 pts. Pts. in first or second relapse or more were 143 and 19, respectively. The first relapse occurred < or > 1 year (8-Rel, 54 pts.; 1-Rel, 88 pts.) after treatment end. HDS included DHAP, cyclophosphamide (7 g/m2), methotrexate (8 g/m2) or MARAC (4 g/m2 x 4 days), etoposide (2 g/m2). The conditioning regimen was BEAM (92), mitoxantrone and melphalan (114) or TBI (20).

**Results:** ASCT was done in all but 9 pts: 4 for peripheral stem cell (PBSC) harvest failure and 5 for disease progression. The mean value of CD34+ reinfused was 6.4 x106/kg PBSC (189 pts.), and 5.3 x 106/Kg for BM transplants (21 pts), unknown in 16. After failure and 5 for disease progression. The mean value of CD 34

**Conclusions:**

- The conditioning regimen was BEAM (92), mitoxantrone and melphalan (114) or TBI (20).
- The first relapse occurred < or > 1 year (8-Rel, 54 pts.; 1-Rel, 88 pts.) after treatment end. HDS included DHAP, cyclophosphamide (7 g/m2), methotrexate (8 g/m2) or MARAC (4 g/m2 x 4 days, etoposide (2 g/m2).
- The conditioning regimen was BEAM (92), mitoxantrone and melphalan (114) or TBI (20).

### 166 PVAG – A NEW REGIMEN IN ELDERLY PATIENTS WITH HODGKIN LYMPHOMA

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**Introduction:** About 20% of patients (pts) diagnosed with Hodgkin lymphoma (HL) are > 60 years (ys) old, 7% > 70 yrs old. While pts aged 60 – 65 yrs with early stage HL have a comparably good treatment outcome, elderly pts with advanced stages demonstrated roughly 50% survival at 3 yrs. In pts > 70 yrs old, treatment outcome is even worse. The most important factor for this poor prognosis appears to be the poor tolerability of chemotherapy, causing substantial dose reduction in rather 50% of elderly pts.

**Methods:** In 2004-2007, the GHSG performed a multicentre trial to investigate a new first-line regimen in elderly pts (60-75 yrs) with advanced stages HL. The study was aimed to improve the standard regimen (ABVD) by lowering treatment toxicity without compromising efficacy. For this reason, we avoided substituted in the newly designed regimen containing prednisone, vinblastin, adriamycin, and gemcitabine (PVAG). Pts received either 6 cycles PVAG in case of complete remission (CR) after 4 cycles, or 8 cycles in case of less CR at time of interim staging. Radiotherapy was given to sites of residual disease. Chemotherapy was applied in a 21 days interval.

**Results:** A total of 61 pts were recruited in 35 collaborating centres. At this point of time, 47 pts with a median age of 69 yrs are available for primary response data. After a median observation time of 7 months, 38 pts (83%) showed CR or partial response, 5 pts showed no response, 3 pts progressive disease. 2 pts stopped the therapy because of intolerable toxicity, 2 pts died. Dose limiting toxicities occurred in 4 pts (mainly leukopenia). Severe adverse events were observed in 19 pts, caused by protocol according hospitalisations in 18 pts. The majority of pts received the full dosage on time.

**Conclusions:** With a generally improved prognosis for patients with HL, interest has increasingly focused on high-risk groups such as elderly patients. PVAG could be demonstrated as safe and effective in this cohort: Because of the encouraging results, the protocol will be further investigated in adult patients with intermediate stages HL (18-60 yrs).

### 167 EARLY REPORT ON THE ACTIVITY OF LENALIDOMIDE IN CHEMOTHERAPY-REFRACTORY HODGKIN LYMPHOMA PATIENTS

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Lenalidomide is an immunomodulatory drug with multiple properties including inhibition of TNFalpha and VEGF (vascular endothelial growth factor), modulation of T-cell activity and impact on the microenvironment. These characteristics suggest that lenalidomide may play a role in the treatment of Hodgkin Lymphoma (HL), since Hodgkin cells are highly dependent on their microenvironment. To investigate the activity in HL, lenalidomide was provided in a named patient program. Patients were eligible if they had active disease and no curative therapeutic options. Lenalidomide was given at 25 mg daily for 21 days, followed by one week rest. Response was assessed according to Chezira criteria. So far, eight are available for safety and efficacy after two cycles of Lenalidomide. Seven were refractory to prior chemotherapy, and one had an early relapse (8 weeks) after allogeneic transplantation. Six patients were male, the age ranged from 20-64 years. The median number of prior treatments was 4 (range 3-7); all patients had received raltretinoid and autologous stem cell transplantation, and two had received an allogeneic transplant. Disease stage was stage II in two patients, stage III in one patient, and stage IV in five patients. Six patients suffered from B-symptoms. Three patients achieved a partial remission and three patients had stable disease as determined by CT. B-Symptoms resolved in all patients. No severe hematological or non-hematological toxicity was documented. Treatment is ongoing in all patients. Plasma samples before treatment and after cycle two have been stored and cytokine levels will be presented. These data indicate that lenalidomide is active in heavily pretreated patients with progressive, refractory HL. It is too early to judge on the duration of the responses. Since therapeutic options in these patients are very limited and their prognosis is very poor, Lenalidomide warrants further evaluation in this setting. The lack of side effects suggest that higher doses might be tolerated in HL patients.

### 168 CLINICAL CHARACTERISTICS AND OUTCOME OF 290 PATIENTS (PTS) WITH HODGKIN'S DISEASE AND HIV INFECTION (HD-HIV) IN PRE- AND HAART (HIGHLY ACTIVE ANTIRETROVIRAL THERAPY) ERA

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**Background:** HD-HIV pts have clinical aggressive characteristics (i.e. advance stage, B symptoms and extranodal involvement) leading to a poor outcome despite the use of standard chemotherapy. The introduction of HAART has improved the survival of AIDS pts. The aim of our study was to compare pathological, clinical characteristics and outcome of HD-HIV in prior-HAART (naïve pts) and HAART era (HAART pts).

**Material and methods:** We collected data of 290 pts with HD-HIV diagnosed and treated in several institutions in Italy and France from 1983 to 2007.

**Results:** HAART pts were significantly older (p<0.0001), had less frequency of B symptoms (p>0.03), and a higher level of leucocytes (p=0.02), neutrophil cell count (p=0.02) and haemoglobin level (p 0.03). In multivariate analysis, the following factors were associated with a shorter survival: histological subtype, extranodal involvement, B symptoms, the prior use of HAART. Factors associated with a shorter time to treatment failure (TTF) in multivariate analysis were International Prognostic Score, the use of HAART, the alcaline phosphatase level.
Conclusions: In our experience, the use of HAART significantly improves the outcome of HD-HIV pts. In our opinion, stratification of patients by prognostic factors of HD and HIV infection is mandatory in order to identify those pts who could benefit by an aggressive chemotherapy regimen similar to that used in HD of the general population.

169  ATTITUDES AND BELIEFS TOWARDS SURVIVORSHIP ISSUES IN HODGKIN'S DISEASE (HD). RESULTS OF FOCUS GROUP DISCUSSIONS WITH PATIENTS TREATED AT STANFORD UNIVERSITY

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Background: The vast majority of patient’s (pts) treated for HD are cured with current treatment strategies. Recently the Institute of Medicine has issued a directive for survivorship care stating that the care of these pts needs to be focused and geared to address specific issues (therapy and non therapy related) as they transition from being cancer pts to cancer survivors.

Methods: We conducted focus group discussions and distributed surveys to a cohort of pts with HD who had completed therapy at least 3 years ago. The aim of these discussions was to find out what attributes of a survivorship care plan would be most important to our survivors, assess the likelihood of compliance in a dedicated Survivorship Care Clinic and how this could be optimized and determine attitudes regarding enrollment in future research studies. 40 pts were contacted via telephone with the goal of having four groups balanced for age, gender, geography and time since treatment.

Results: 30 pts (17 male and 13 female) median age 46 y (range: 35-76) participated in 4 focus groups led by professional moderators. Median time since treatment was 10 y (range: 3-40). 25 pts had been treated with the Stanford V regimen (initiated 1989) and 5 on earlier protocols. Seven pts had relapsed and had received salvage therapy. Levels of interest in response to survey questions are shown in the table.

<table>
<thead>
<tr>
<th>Level of Interest</th>
<th>Slight/Moderate N</th>
<th>High/Enthusiastic N</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Attributes of Survivorship Care</strong></td>
<td></td>
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</tr>
<tr>
<td>Risk of relapse</td>
<td>8</td>
<td>22</td>
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<tr>
<td>Risk of second cancer</td>
<td>4</td>
<td>26</td>
</tr>
<tr>
<td>Effects on normal organs</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td>Psychological aspects</td>
<td>15</td>
<td>13</td>
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<tr>
<td>Social functions</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Participation in research</td>
<td>4</td>
<td>26</td>
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<tr>
<td><strong>Models of Survivorship Care</strong></td>
<td></td>
<td></td>
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<tr>
<td>Physician led</td>
<td>10</td>
<td>20</td>
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<tr>
<td>Nurse led</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Shared with primary MD</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>Virtual web based</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td><strong>Receiving a Survivorship Care Plan</strong></td>
<td></td>
<td></td>
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<tr>
<td>Treatment Summary</td>
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<td>29</td>
</tr>
<tr>
<td>Personalized care plan</td>
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<td>28</td>
</tr>
<tr>
<td><strong>Method of information delivery</strong></td>
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<tr>
<td>Web based or DVD</td>
<td>8</td>
<td>22</td>
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<tr>
<td>Dedicated Survivorship House</td>
<td>22</td>
<td>8</td>
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</tbody>
</table>

Conclusions: Receipt of a treatment summary and a personalized survivorship plan was highly desired by participants. Our pts, who were highly selected were more interested in learning about risks to their ongoing physical health than psychological or social function. Most pts preferred physician led models (oncologist or shared with primary care) and were highly motivated and interested in research participation. Web or DVD based resources as a method to obtain relevant information was preferred over a dedicated survivorship house concept. These results will be utilized in prioritizing our efforts towards a formal survivorship program for HD pts.