approaches to repeat screening at critical junctures such as treatment completion and relapse.

Patients agreed to further referrals to:	% of patients
Lung support nurse	75
Further input from doctor	70
Occupational therapy	49
Social work	39
Sources of additional written information	37
Physiotherapy	29
Dietician	27
Psychology/Psychiatry	13
Pastoral Care	8

B6-06 **Health Services, Supportive Care & QOL, Tue, 13:45 - 15:30**

Assessing the quality of a lung cancer service

O'Rourke, Noelle

West of Scotland Lung Cancer Network, Glasgow, UK

Background: In 2002 national cancer registry based audit data demonstrated that for lung cancer in Scotland there were statistically significant survival differences depending upon where the patient lived. This correlated with data on patterns of care, confirming differences in use of active cancer treatment by geographical area. The West of Scotland Lung Cancer Network was established in 2002 with the aim of delivering consistent high quality care across all hospital units with equity of access to lung cancer specialists. Prospective lung cancer audit was established for the regional network in 2003 with a dataset including demographic data, treatment details and outcome. This current study aims to assess changes in patterns of care since 2002 and compares the six geographical areas within the region on quality of lung cancer service.

Method: On 2005 audit data eight indicators of quality of care were used to compare the current service across geographical areas:

1. Comprehensive lung cancer care to local population as measured by case ascertainment in audit compared to national cancer registry data
2. Multidisciplinary (MDT) team discussion of patient management
3. Histological diagnostic rate
4. Surgical resection rate
5. Chemotherapy use in small cell lung cancer (SCLC) patients
6. Patients receiving no active anti-cancer therapy
7. Recruitment to clinical trials
8. One year survival

The national audit data published in 2002 provided a baseline comparison.

Results: Case ascertainment for the region was 82.8%, but ranged from 63.4-96.1% across the six areas. MDT input was achieved in mean 84.2% patients but ranged from 60.4-96.5%. Histological diagnosis mean rate was 81.9%, range 76.9-86.4%. Surgical resection varied from 6.5-22% (mean 10.7%). Chemotherapy was used in 62.4% SCLC patients but ranged from 35.7-73.3%. In the 2002 data 43% patients received no active treatment which had fallen to a mean of 25% in 2005 but areas varied 19.4-35.1%. Recruitment to trials was poor average 1.6%, range 0-4.2%. One year survival for 2002 ranged from 21.6-25.8%, but for 2004 patients across the region ranged from 26.7-33%.

Conclusions: With the development of a lung cancer network the treatment rates and survival for lung cancer can be shown to be improved. Geographical differences in care still persist however and this assessment will be used to stimulate further improvements.

B6-07 **Health Services, Supportive Care & QOL, Tue, 13:45 - 15:30**

Symptom assessment in small cell lung cancer (sclc) in a randomized trial: a psychometric analysis of Patient Symptom Assessment in Lung Cancer (PSALC)

Chen, Lei[1] Antras, Lucia[1] Duh, Mei Sheng[1] Neary, Maureen[2] O'Brien, Mary E.[3]

[1] Analysis Group, Inc., Boston, MA, USA [2] GlaxoSmithKline, Collegeville, PA, USA [3] Royal Marsden Hospital, Sutton, UK

Background: Lung cancer symptoms can be very burdensome for patients with SCLC and can result in impairment in quality of life and health status. PSALC is a symptom scale developed for use in patients with SCLC for assessment of 9 symptoms (shortness of breath, cough, chest pain, hemoptysis, appetite loss, sleep interference, hoarseness, fatigue, interference with daily activities) scored from 1 (not at all) to 4 (very much), but it has not been formally validated. The objective of this study is to evaluate the validity of the PSALC through a psychometric analysis of trial data.

Methods: Data were analyzed from a randomized, open-label, multicenter trial with 71 patients with SCLC receiving oral topotecan with best supportive care (BSC) and 70 patients receiving BSC alone. PSALC and EQ-5D were administered to patients at baseline and at 3-week intervals at subsequent visits. Internal consistency, construct validity, reliability, and responsiveness to change in clinical status were evaluated.

Results: Factor analysis using baseline PSALC evaluations (n=132) indicated that all 9 symptom questions can be summarized as one factor, therefore, PSALC total score was used for psychometric analysis. Weighted Cronbach's alpha from all visits was 0.78. Construct validity was supported by the association of higher PSALC total score (worse symptoms) with worse ECOG performance status (Table). The PSALC total score was also significantly correlated with EQ-5D utility index and EQ-5D VAS score at baseline and at follow-up visits (Pearson correlation coefficient [CC]=-0.598 with EQ-5D utility index; Pearson CC=-0.594 with EQ-5D VAS score; using evaluations at all time points; both $p<0.0001$). Reliability was supported by intraclass CC of 0.68 for PSALC total scores evaluated before any change in clinical status, and concordance CC of 0.69, calculated using PSALC total scores at baseline and before first visit. The PSALC total score was responsive to change in clinical status from baseline to tumor response (responsiveness statistic [RS] =-0.99) and to tumor progression (RS=0.94).

ECOG	Baseline	Visit 1	Visit 2	Visit 3	Visit 4
0	12.3	14.7	13.6	13.8	12.7
1	16.4	15.5	14.6	14.1	15.2
2	17.6	17.8	16.3	16.1	16.9
3	n/a	22.4	22.8	19.6	20.7
p-value	0.0002	0.0017	<0.0001	0.0048	0.0011
N	132	98	77	66	49

Conclusions: Retrospective analysis of trial data suggests that PSALC is a reliable, valid, and responsive scale for measuring SCLC symptoms. If feasible in SCLC population, a prospective validation study could be used to further evaluate the validity of this symptom scale.

Session B7: BSTB: Molecular Diagnostics & Pathology

Tuesday, September 4

B7-01 **BSTB: Molecular Diagnostics & Pathology, Tue, 13:45 - 15:30**

Aberrant pattern of histone H4 modification in human lung carcinoma

Brambilla, Elisabeth[1] van den Broeck, Arnaud[1] Eymin, Béatrice[1] Lantuejoul, Sylvie[2] Moro-Sibilot, Denis[2] Brambilla, Christian[2] Gazzeri, Sylvie[1]

[1] Lung Tumor Research Group INSERM U823, University Joseph Fourier, Grenoble, France [2] INSERM U823, University Joseph Fourier, Grenoble, France

Background: Post-translational modifications in the tails of nucleosomal core histones are emerging as important signalling processes controlling a wide variety of functions. Indeed they play a crucial role in chromatin packaging, gene expression and genome stability. Therefore, perturbation of this epigenetic information is likely to be involved in the development of cancer. Although some studies identified an altered activity of histone-modifying enzymes in tumors, little is known about the post-translational modifications of histones in these malignancies.

Methods: By using immunohistochemistry, we studied the pattern of histone H4 modifications in a series of 100 primary non small cell lung tumors comprising 51 squamous carcinoma and 49 adenocarcinoma. Specific antibodies recognizing acetylated histone H4 at positions K5, K8 and K16 and trimethylated histone H4 at position K20 were used on frozen tissue sections with an automated immunostainer Ventana in order to standardize the staining. Normal lung epithelial cells (alveolar and bronchial basal cells) were taken as internal controls and their score used for determination of the cut off score to discriminate between positive (score at least equal to normal) and negative (score lower than normal) cases.

Results: Our data show that, as compared to normal lung, lysines 5 and 8 of histone H4 are hyperacetylated in 48% and 40% of all tumors respectively, more frequently in squamous carcinoma than in adenocarcinoma (p=0.009 and p=0.0002 respectively). In contrast, acetylation at Lys16 and trimethylation at Lys20 are lost in 52% and 47% of the tumors respectively. Across histological types loss of trimethylation at Lys20 is more frequent in squamous carcinoma than in adenocarcinoma (p=0.0002), is associated with advanced stage (p=0.018) and nodal metastasis (p=0.01) and correlates with a poor survival among stade I (p=0.026). Importantly, in adenocarcinoma, loss of trimethylation at Lys20 is associated with advanced stage (p=0.006) and correlates with a poor survival among stage I-II (p=0.0001) and N0 versus N1-2 (p=0.013) tumors. Furthermore, the double loss of acetylation at Lys16 and trimethylation at Lys20 is associated with a shorter survival in these patients as compared to the presence of either one or none of these alterations.

Conclusion: These data provide the first evidence of a global aberrant pattern of histone H4 modification in lung tumors with hyperacetylation of Lysines 5 and 8 and loss of acetylation of lysine 16 and of trimethylation of Lysine 20. The frequent loss of lysine 20 trimethylation in squamous carcinoma, independently of the stage, suggests that it could be an early event in the carcinogenesis of this tumor type. In contrast, loss of lysine 20 trimethylation is less frequent in adenocarcinoma but correlates with a poor prognosis suggesting a role in the progression of these tumors.

B7-02 **BSTB: Molecular Diagnostics & Pathology, Tue, 13:45 - 15:30**

Identification of differentially methylated CpG Islands in the early stage of human pulmonary adenocarcinoma

Sun, Weihong; Iijima, Tatsuo; Kano, Junko; Anami, Yoichi; Inadome, Yukinori; Morishita, Yukio; Okubo, Chigusa; Noguchi, Masayuki

Department of Pathology, Institute of Basic Medical Sciences, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tsukuba City, Japan

Background: In the development of cancer, a series of tumor suppressor genes is inactivated by point mutation and chromosomal deletion. Aberrant methylation of CpG islands has recently been shown to serve as an alternative way of inactivating such genes in cancer. Methylation of cytosine residues in CpG dinucleotides is an extremely important epigenetic modification of the eukaryotic genome that affects various cell processes. Methylation is known to play an important role in neoplasia by inactivating tumor suppressor genes such as Rb, p16, and estrogen receptor. In this study we used CpG island amplification and suppression subtractive hybridization to identify the aberrant methylation of CpG islands in A/J mouse lung adenoma, in order to clarify whether a hypermethylated homologue gene exists in human pulmonary adenocarcinoma.

Methods: NNK (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone)-induced A/J mouse lung adenoma and normal tissue were used in this study. The histology of A/J mouse adenoma mimics the early stage of human pulmonary adenocarcinoma. The genomic DNA was extracted using standard procedures. The PCR-based methylated CpG island amplification (MCA) technique was used for detection of methylated CpG islands. Suppression subtractive hybridization (SSH) and differential screening (DS) were used to identify the differentially methylated sequence in A/J mouse lung adenoma tissue. For the genes selected after SSH and DS analysis, quantitative Real-time PCR was used to check their expression level in A/J mouse lung adenoma tissue and normal tissue. Using homoloGene software, human homologue genes were then detected. Real-time PCR was also performed to check the expression level of these genes in human lung adenocarcinoma and normal lung tissue. Bisulfite genomic sequencing was done to confirm the methylation status of these genes in the promotor area.