nodes in 43%, brain in 25%, bone in 28%, pleural in 21%, and adrenal in 8%.
Results: All but 4 pts received systemic treatment for their IIIB/IV disease. Seventy-one pts received as first-line a platinum-based doublet (among them 46 were treated with cisplatin + gemcitabine and 5 received bevacizumab too), 6 a platinum-based triplet, 8 a single-agent therapy. In evaluable patients we observed 3 complete responses and 21 partial responses. Forty eight pts received a second-line treatment (consisting of non cross resistant chemotherapy in 31 pts and of TKIs in 17), 27 a third-line (16 chemotherapy, 11 TKi) and 11 a fourth-line treatment (2 received chemotherapy, 9 TKi). The MS is 19 mos with a 62.5% 1-y OS.
Conclusions: Our experience confirmed that $\leqslant$ 40 years IIIB/IV NSCLC pts presented survival outcomes better than expected in the overall population.

9148 POSTER

Incidence of Bone Metastases and Skeletal-related Events in Patients With Advanced Lung Cancer − Results of a Multicenter, Prospective, Cohort Study (CSP-HOR13)

N. Seki[1], K. Eguchi[1], N. Katakami[2], H. Kunikane[3], K. Takeda[4], K. Takayama[5], T. Sawa[6], H. Saito[7], M. Harada[8], Y. Ohashi[9]. *[1]Teikyo University School of Medicine, Division of Medical Oncology, Tokyo, [2]Institute of Biomedical Research and Innovation, Division of Integrated Oncology, Kobe, [3]Yokohama Municipal Citizen's Hospital, Departments of Respiratory Medicine, Yokohama, [4]Osaka City General Hospital, Department of Clinical Oncology, Osaka, [5]Graduate School of Medical Sciences Kyushu University, Research Institute for Diseases of the Chest, Fukuoka, [6]Gifu Municipal Hospita, Respiratory Department, Gifu, [7]Aichi Cancer Center Aichi Hospital, Department of Respiratory Medicine, Aichi, [8]National Hospital Organization Hokkaido Cancer Center, Department of Respiratory Medicine, Hokkaido, [9]The University of Tokyo, Department of Biostatistics School of Public Health, Tokyo, Japan*

Background: The incidence of bone metastases (BM) in patients with advanced lung cancer based on prospective study is not known so far despite the frequent complication. BM can be associated with skeletal-related events (SREs), which include pathologic fracture, need for surgery or radiation to bone, spinal cord compression, and hypercalcemia of malignancy. The aim of our study is to investigate prospectively the incidence of BM, the incidence and types of SREs, time interval between BM and SREs, influence of SREs on QOL, and predictive factors for SREs.
Materials and Methods: Eligibility criteria included newly diagnosed patients with stage IIIB or IV lung cancer, age over 20 years old, and written informed consent. Staging of lung cancer was evaluated with chest and abdominal CT, brain CT or MRI, and bone scintigraphy or PET/CT. Patients were closely followed up every 4 weeks to see if they developed SREs. During the follow-up, radiological examinations were performed every 4 weeks for the chest and abdomen, and every 6 months for the brain and bone. Treatment for lung cancer and use of zoledronate were at the discretion of the investigator. QOL questionnaire was carried out at enrollment, 3 months, and 12 months. Serum concentrations of Alb, Ca, PTHrP, bone-specific alkaline phosphatase (BALP), and type I collagen cross-linked N-telopeptides (NTx) were measured at enrollment.
Results: Two hundred and seventy four patients were enrolled into the study between Apr. 2007 and Dec. 2009 from 12 institutions. Median age was 68 years, small cell/non-small cell=77/197, IIIB/IV=73/124, M/F=193/81, PS 0/1/2/3−4=76/171/23/4. Median follow-up period was 10.3 months (0–27.2 months). Seventy eight patients (28% of all and 62% of stage IV) had BM already at enrollment. Among them, 24 had SREs concomitantly and additional 11 developed SREs during the follow-up. Among 196 patients without initial BM, 31 developed BM, and 14 of these 31 patients developed SREs during the follow-up. Eventually, 49 (18%) of all 274 patients developed 64 SREs, consisting of pathologic fracture in 13 (5%) cases, radiation to bone in 42 (15%) cases, spinal cord compression in 3 (1%) cases, and hypercalcemia in 6 (2%) cases. One-year incidence rate of SREs from the diagnosis of BM was 50%.
Conclusions: In 274 patients with advanced lung cancer, the incidence of BM and SREs was 28% and 9% at initial diagnosis, respectively, whereas BM and SREs eventually developed in 40% and 18% during the follow-up, respectively. Furthermore, details of predictive factors for SREs and influence of SREs on QOL will be provided.

9149 POSTER

Diagnosis of Bone Metastasis in Patients With Lung Cancer Using Urinary and Serum Collagen Type I Telopeptide (NTx)

H. Daga[1], M. Tamiya[2], S. Tokunaga[1], H. Okada[1], M. Kobayashi[2], N. Okamoto[2], S. Sasada[2], H. Suzuki[2], T. Hirashima[2], K. Takeda[1]. *[1]Osaka City General Hospital, Clinical Oncology, Osaka, [2]Osaka Prefectual Medical Center for Respiratory and Allergic Diseases, Respiratory Medicine, Osaka, Japan*

Background: Many cancers metastasize to bone. Bone metastasis may cause an increase in bone resorption due to direct effects of the tumour itself or osteoclastic activation. This study evaluates the bone resorption biomarkers urinary NTx (uNTx) and serum NTx (sNTx) for the diagnosis of bone metastasis in patients with lung cancer.
Methods: uNTx and sNTx were measured in 100 patients with lung cancer and 50 control patients with benign respiratory diseases using the uNTx:OSTEOMARK™ and sNTx:OSTEOMARK™ serum NTx assays (Inverness Medical Japan). Bone metastasis was characterized by scintigraphy. The extent of disease (EOD) was determined by the number of sites of bone metastasis. Area under the curve (AUC) for receiver operating characteristic (ROC) analysis was used to evaluate the detection of bone metastasis. Sensitivity and specificity of uNTx and sNTx to detect bone metastasis were calculated using cutpoints of 64 nM BCE/mM Cr for uNTx and 22 nM BCE/mM Cr for sNTx. All patients were required to provide written informed consent.
Results: Patients with bone metastasis had significantly higher levels of both uNTx and sNTx (uNTx; 93.2$\pm$105.1 nM BCE/mM Cr., sNTx; 24.0$\pm$14.6 nM BCE/L) vs. lung cancers without bone metastasis (uNTx; 51.6$\pm$26.8 nM BCE/mM Cr., sNTx;17.2$\pm$4.1 nM BCE/L), or benign respiratory diseases (uNTx; 42.8$\pm$21.8 nM BCE/mM Cr., sNTx; 16.8$\pm$7.9 nM BCE/mM Cr.). There was good correlation between uNTx and sNTx (R = 0.807). ROC AUC for the detection of bone metastasis was 0.743 for uNTx and 0.712 for sNTx. The sensitivity and specificity for the diagnosis of bone metastasis using uNTx was 48.0% and 86.0%, and using sNTx was 40.0% and 87.0%, respectively. Levels of uNTx and sNTx were increased in patients classified as EOD grade I compared to controls and in patients classified as EOD grade II or greater, compared to patients classified as EOD grade I.
Conclusions: Both biomarkers may have value as an aid in the diagnosis of bone metastasis in patients with lung cancer.

9150 POSTER

Testing Practices for EGFR and KRAS in Advanced Non-small Cell Lung Cancer in a Comprehensive Cancer Care Setting in Korea

Y. Choi[1], J. Han[1], J. Cho[2], E. Guallar[3], B. Parasuraman[4], G. Lee[5], K. Park[6], J. Lee[6], J. Sun[6], Y.M. Shim[5]. *[1]Samsung Medical Center, Department of Pathology, Seoul, [2]Samsung Medical Center, Cancer Education Center, Seoul, Korea; [3]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, [4]Astra Zeneca, Health Economics and Outcome Research, Willmington, USA; [5]Samsung Medical Center, Department of Thoracic and Cardiovascular Surgery, Seoul, [6]Samsung Medical Center, Division of Hematology-Oncology Department of Medicine, Seoul, Korea*

Background: Guidelines for management of non-small cell lung cancer (NSCLC) patients strongly recommend testing for EGFR. These recommendations are particularly relevant in Asian countries that have a higher prevalence of EGFR mutation positive patients, but also in Western countries despite the lower mutation prevalence. The objective of this study was to explore current testing practice of EGFR and KRAS mutation in advanced NSCLC patients in a large comprehensive cancer center in Korea.
Material and Methods: Retrospective cohort study of stage IIIb/IV NSCLC patients 18 years of age or older who attended Samsung Medical Center in Seoul, Korea, from January 2007 through July 2010. Trained oncology nurses reviewed electronic medical records for clinical and pathology data. Mutation status was assayed using bidirectional direct sequencing.
Results: The study included 1,527 patients with a median age of 60.5 years (interquartile range 52.4 to 68.0), 37.3% were female and 52.7% never smokers. The most common histology was adenocarcinoma (70.3%), followed by squamous cell carcinoma (18.1%). The proportions of patients tested for EGFR and KRAS mutations were 38.0% and 25.0% respectively; 364 (23.8%) study participants were tested for both markers. For EGFR testing, the proportion of patients tested in 2007, 2008, 2009, and 2010 were 5.2%, 17.6%, 37.1%, 40.0% respectively. The median time elapsed between confirmed diagnosis of cancer and receiving EGFR testing results was 21 days. EGFR testing was most frequently ordered by oncologists (57.7%) and pulmonologists (31.9%), followed by thoracic surgeons (6.6%).

EGFR testing was more commonly done among women, younger patients, stage IV disease, non-smokers, and adenocarcinoma histology. Of 581 cases successfully tested for EGFR mutations, 211 (36.3%) were positive, including 120 with exon 19 deletions and 63 with exon 21 L858R mutations. Of 381 cases tested for KRAS mutations, 30 (7.9%) were positive, including 25 G12 mutations. Patients who were EGFR mutation positive were more likely to be women, never smokers, never drinkers and to have adenocarcinma histology.
Conclusions: About 40% and 25% of the patients had tests for EGFR and KRAS mutations, respectively. The proportion of EGFR testing is increasing over time, but formal guidelines for NSCLC diagnosis and treatment should provide specific guidance on biomarker testing required in NSCLC.

9151 POSTER

Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor (EGFR-TKI) Treatment and Radiotherapy (RT) for Central Nervous System (CNS) Are Favorable Prognostic Factors for Carcinomatous Meningitis (CM) in Lung Adenocarcinoma (AD)

Y. Nakamura[1], T. Takahashi[1], H. Kenmotsu[1], T. Naito[1], H. Murakami[1], A. Tsuya[1], M. Endo[2], R. Watanabe[3], T. Nakajima[3], N. Yamamoto[1]. *[1]Shizuoka Cancer Center, Division of Thoracic Oncology, Shizuoka-pref., [2]Shizuoka Cancer Center, Division of Diagnostic Radiology, Shizuoka-pref., [3]Shizuoka Cancer Center, Division of Pathology, Shizuoka-pref., Japan*

Background: As a result of recent advances in systemic chemotherapy for advanced lung AD, the numbers of patients with CM tend to increase. Although various treatment strategies have already been applied to CM, there is still no treatment proved to be effective. The aim of this study was to identify prognositic factors of CM in lung AD.
Methods: We retrospectively reviewed 68 lung AD patients with CM diagnosed by cytology and/or contrast-enhanced MRI at Shizuoka Cancer Center from September 2002 to March 2011.
Results: The patient characteristics were as follows: median age (range), 64.5 years (35−80); females, 30 (44%); non-smokers, 24 (35%); performance status (PS) 0−2 at the time of diagnosis of CM, 38 (55%); EGFR gene status, mutant 10 (15%), wild type 15 (22%), unknown 43 (63%); number of patients treated with EGFR-TKIs after the diagnosis of CM, 37 (54%); number of patients treated with RT for CNS after the diagnosis of CM, 32(47%). The median survival time (MST) after the diagnosis of CM (range) was 121 days (10–817 days). A multivariate analysis showed good PS (hazards ratio (HR), 0.40: 95% confidence interval (CI), 0.22–0.73: p = 0.0031), EGFR-TKI treatment after the diagnosis of CM (HR, 0.21: 95% CI, 0.10–0.44: p < 0.0001) and RT for CNS after the diagnosis of CM (HR, 0.41: 95% CI, 0.21–0.79: p = 0.0079) were good prognostic factors, and EGFR wild type was a poor prognostic factor (HR, 2.35: 95% CI, 1.10–4.93: p = 0.0274). In an analysis of 37 patients treated with EGFR TKIs after the diagnosis of CM, there was no significant difference of survival between 21 patients treated with EGFR-TKI for the first time after the diagnosis of CM and 16 patients treated with EGFR-TKI both before and after the diagnosis of CM (240 vs 218 days,p = 0.9354). MST of 9 patients who were treated with gefitinib before the diagnosis of CM and with erlotinib after the diagnosis was significantly longer than that of 7 patients who were treated with gefitinib both before and after the diagnosis of CM (407 vs 205 days, p = 0.0081). 15 patients treated with both RT for CNS and EGFR-TKI after the diagnosis of CM had longer survival compared to 22 patients without RT for CNS (301 vs 123 days, p = 0.0069).
Conclusion: Taking the EGFR gene status into consideration, EGFR-TKI treatment, especially by erlotinib, combined with RT for CNS may be a promising therapeutic approach to improve the prognosis of lung AD patients with CM.

9152 POSTER

Comparative Value of Various Chemotherapy Regimens in 1st-line Treatment of Adenocarcinoma of the Lung

J.R. Hoverman[1], S.R. Sheth[1], M. Clayton[1], M.A. Neubauer[1], M.A. Kolodziej[1], R.W. Anderson[1], R. Beveridge[1]. *[1]US Oncology, Pathways Task Force, The Woodlands, USA*

Background: Continuing a series of studies mining a large US Oncology (USON) electronic health record (EHR) database (iKnowMed™) regarding non-small cell lung cancer (NSCLC) we sought to answer three questions: 1) Is there a difference in value among current chemotherapy regimens for adenocarcinoma alone? 2) Does large cell carcinoma respond differently than adenocarcinoma to current regimens? 3) Can we assess the cost effectiveness of the newest regimen − carboplatin/paclitaxel followed by maintenance pemetrexed (CPMPem)?
Methods: EHR data from USON outpatient community cancer centers was reviewed. Advanced NSCLC patients with adenocarcinoma or large cell carcinoma and documented 1st-line treatment with carboplatin + paclitaxel (CP), or carboplatin + paclitaxel + bevacizumab (CPB), or cisplatin + pemetrexed (CisPem), or CPMPem were identified between July 1, 2008 to August 31, 2010. Cytotoxic treatment and estimated 1-year and 2-year survivals were evaluated. Patients were excluded if they had participated in a clinical trial, had received 1st-line with cytotoxic treatment other than above, non-adenocarcinoma or non- large cell carcinoma histology, and/or insufficient data. Survival was estimated using the Kaplan–Meier method.
Results: 1) In the adenocarcinoma cohort, 339 pts received CP, 395 CPB, and 104 CisPem. Median overall survival (OS): 10.1, 17.3, 15.8 months, respectively (P < 0.05 for both CP vs. CPB and CP vs. CisPem). Estimated 2-year survivals were CP 21%, CPB 37%, and CisPem 49%. P = 0.26 for OS CPB vs CisPem. Previous calculations (ISPOR May 2010) indicated CPB was twice as costly as CisPem. 2) Median OS for the large cell carcinoma cohort was 10.7 months for 113 pts; 62 received CP, 51 received bevacizumab or pemetrexed regimens. P = 0.38 for OS for CP vs. any bevacizumab or pemetrexed regimens; P = 0.18 for all large cell carcinoma vs adenocarcinoma CP. 3) 48 cases existed of CP followed by pemetrexed. Due to coding discrepancies, no electronic logic could separate CP followed by pemetrexed to differentiate maintenance vs 2nd-line treatment.
Conclusions: 1) CPB and CisPem are markedly superior to CP in lung adenocarcinoma. CisPem is more cost effective. 2) Large cell carcinoma responds no better than adenocarcinoma to CP, and the benefit of new regimens is unproven. 3) We could not assess the benefit of CPMPem due to coding errors, perhaps a peculiar problem of maintenance regimens, adding a note of caution to electronic databases.

Oral Presentations (Sat, 24 Sep, 11:15−12:40)
Haematological Malignancies

9200 ORAL

A Phase 3 Study Comparing Melphalan-Prednisone-Lenalidomide (MPR) With High-dose Melphalan and Autologous Transplantation (MEL200) in Newly Diagnosed Patients With Multiple Myeloma (MM)

A. Palumbo[1], F. Cavallo[1], F. Di Raimondo[2], T. Caravita di Toritto[2], S. Grammatico[2], P. Corradini[2], P. Omedè[1], D. Ben Yehuda[3], A. Nagler[4], M. Boccadoro[1]. *[1]AOU S. Giovanni Battista, Myeloma Unit Division of Hematology University of Torino, Torino, [2]GIMEMA, Italian Multiple Myeloma Network, Italy, Italy; [3]Hadassah Medical Center, Hadassah Medical Center, Jerusalem, [4]Chaim Sheba Medical Center, Hematology Division & Cord Blood Bank, Tel-Hashomer, Israel*

Background: The introduction of new drugs has changed the treatment paradigm of multiple myeloma (MM) and questioned the role of autologous stem-cell transplantation (ASCT). The aim of the present prospective randomized study is to compare conventional chemotherapy plus new drugs [melphalan-prednisone-lenalidomide (MPR)] with tandem high-dose melphalan (MEL200) and ASCT in newly diagnosed MM patients (pts).
Materials and Methods: Four-hundred two pts were enrolled and received induction treatment with four 28-day cycles of lenalidomide (25 mg, days 1−21) in combination with low-dose dexamethasone (40 mg, days 1, 8, 15, 22). After induction therapy, 202 pts were randomly allocated to MPR treatment [six 28-day cycles of melphalan (0.18 mg/kg days 1−4), prednisone (2 mg/kg days 1−4) and lenalidomide (10 mg days 1−21)]; the other 200 pts were assigned to receive MEL200 (tandem melphalan 200 mg/m^2 with stem-cell support). Progression-free survival (PFS) was the primary endpoint of this study.
Results: Similar response rates were reported in the two groups (MPR vs MEL200): at least very good partial response (60% vs 58%, p = 0.24) and complete response (CR) (20% vs 25% p = 0.49). After a median follow-up of 20 months, the 18-month PFS was 68% in MPR and 78% in MEL200 (HR = 0.58, p = 0.006). The 18-month overall survival (OS) was similar in the two groups (91% vs 95%, respectively; p = 0.073). In the MPR and MEL200 groups, the respective incidence of grade 3−4 (G3−4) neutropenia was 55% vs 89% (p < 0.001); G3−4 infections were 0% vs 17% (p < 0.001); G3−4 gastrointestinal toxicity was 0% vs 21% (p < 0.001); DVT was 2.44% vs 1.13% (p = 0.43); the incidence of second tumours was 0.005% in both arms.
Conclusions: MEL200 led to longer PFS compared with MPR, despite MEL200 being associated with a significantly higher toxicity-profile. This is the first report showing a PFS advantage for ASCT in comparison with combinations including new drugs. At present, no significant OS differences between the two groups were detected, and longer follow-up is needed.