($p = 0.019$), CD25 ($p = 0.003$), CD127 ($p = 0.031$), Foxp3 ($p < 0.0001$) and TGF-β1 ($p < 0.0001$) between patients and controls. Pairmatched samples comparing pre and post-treatment expression of TGF-β1 showed that it was significantly reduced after chemotherapy. Additionally, patients with higher ratios (baseline/post-treatment) of CD4 and TGF-β1 were associated with local metastasis and progression, respectively. Survival analysis revealed that patients with combined high expression of CD25 and low expression of CD127 (reflecting a Treg phenotype), had significantly reduced TTP (median 2.40 months *vs* 5.47 months, $p = 0.001$) and a trend in OS (median 3.87 months *vs* 9.80 months, $p = 0.078$).

Conclusion: Based on gene expression analysis, it seems that the presence of a "Treg profile" in peripheral blood is associated with a poor prognosis in patients with advanced NSCLC.

This work was supported in part, by a grant [RD06/0020/1024] from Red Temática de Investigación Cooperativa en Cáncer, RTICC, Instituto de Salud Carlos III (ISCIII), Spanish Ministry of Science and Innovation & European Regional Development Fund (ERDF) "Una manera de hacer Europa".

9132 POSTER

Efficacy Outcomes in First-line Treatment of Advanced NSCLC With Gefitinib (G) vs Carboplatin/paclitaxel (C/P) by Epidermal Growth Factor Receptor (EGFR) Gene-copy Number Score and by Most Common EGFR Mutation Subtypes − Exploratory Data From IPASS

J. Yang[1], Y.L. Wu[2], N. Saijo[3], S. Thongprasert[4], D.T. Chu[5], Y.M. Chen[6], E. Duffield[7], Y. Rukazenkov[8], T.S.K. Mok[9], M. Fukuoka[3]. *[1]Taiwan University Hospital & College of Medicine, National Taiwan University, Taipei, Taiwan; [2]Guangdong General Hospital, Guangdong Lung Cancer Institute Guangdong Academy of Medical Sciences, Guangzhou, China; [3]Kinki University School of Medicine, Department of Oncology, Osaka-Sayama, Japan; [4]ChiangMai University, Maharaj Nakorn ChiangMai Hospital, ChiangMai, Thailand; [5]Chinese Academy of Medical Sciences, Cancer Institute and Hospital, Beijing, China; [6]Taipei Veterans General Hospital, Chest Department, Taipei, Taiwan; [7]AstraZeneca, Biostatistics, Macclesfield, [8]AstraZeneca, Research and Development, Macclesfield, United Kingdom; [9]The Chinese University of Hong Kong, State Key Laboratory in Oncology in South China Sir YK Pao Center for Cancer Department of Clinical Oncology, Hong Kong, China*

Background: IPASS (NCT00322452) demonstrated significantly improved progression-free survival (PFS) and objective response rate (ORR) with first-line G *v* C/P. EGFR mutation was a strong predictive biomarker for PFS benefit and tumour response to first-line G *v* C/P. PFS was prolonged for G *v* C/P in both common activating mutation subtypes. Here we report exploratory analyses of PFS and ORR in patients (pts) with high EGFR gene-copy number (high gene polysomy or gene amplification), and overall survival (OS) by most common EGFR activating mutation subtypes (Exon 19 deletion; L858R point mutation).

Methods: EGFR gene-copy number was determined by fluorescence in-situ hybridisation. High EGFR gene-copy number was defined as high gene polysomy (score 5; $\geqslant$4 copies in $\geqslant$40% of cells) or gene amplification (score 6; gene:chromosome $\geqslant$2, or $\geqslant$15 copies per cell in $\geqslant$10% cells). For each of these groups, hazard ratios (HRs; G:C/P) and 95% CIs were estimated for PFS using a Cox proportional hazards model adjusted for WHO PS (0, 1 *v* 2), smoking history (never *v* light ex-smoker) and gender. Odds ratios (ORs) and 95% CIs were estimated for ORR using a logistic regression model adjusted for the same covariates. EGFR mutations were detected using an amplification mutation refractory system with an EGFR detection kit. For pts with Exon 19 deletion or L858R mutation, HRs and 95% CIs were estimated for OS using a Cox proportional hazards model adjusted for the same covariates as PFS.

Results: 406 (of 1217 randomised) pts had known EGFR-gene-copy number biomarker status: 83 with gene amplification; 166 with high gene polysomy. PFS and ORR outcomes for G *v* C/P in pts with gene amplification: PFS HR 0.46, 95% CI 0.28–0.77; ORR OR 4.46, 95% CI 1.57–12.68; and in pts with high gene polysomy: PFS HR 0.77, 95% CI 0.53–1.11; ORR OR 1.46, 95% CI 0.79–2.71. Incidence of co-existing EGFR mutation was higher with gene amplification (86.7%) than high gene polysomy (71.1%). 261 pts had EGFR mutation-positive tumours: 140 with Exon 19 deletion; 111 with L858R. HRs for OS were 0.79 (95% CI 0.54–1.15) for Exon 19 deletion and 1.44 (95% CI 0.90–2.30) for L858R mutation.

Conclusions: PFS and ORR were improved with G *v* C/P in both gene-copy number score groups, with greater benefit with G in the gene amplification group. This was probably driven by an overlap with co-existing EGFR mutation, a known predictive biomarker for improved PFS and ORR with G in this setting.

9133 POSTER

Association Between TS, DHFR, and GARFT mRNA Expression and Efficacy of Pemetrexed in Advanced Non-small Cell Lung Cancr Patients

T. Shimizu[1], Y. Nakanishi[2], Y. Nakagawa[1], T. Sugane[1], I. Tsujino[1], T. Oinuma[2], N. Takahashi[1], S. Hashimoto[1], N. Nemoto[2]. *[1]Nihon University School of Medicine, Respiratory Medicine, Tokyo, [2]Nihon University School of Medicine, Pathology, Tokyo, Japan*

Background: Pemetrexed (PMT), a multitargeted antifolate drug, inhibits three key folate enzymes: thymidylate synthetase (TS), dihydrofolate reductase (DHFR), and glycinamide ribonucleotide formyltransferase (GARFT). PMT is effective in non-small-cell lung cancer (NSCLC) patients with non-squamous cell carcinoma. TS expression is lower in adenocarcinoma compared with squamous cell carcinoma. The relationship between clinical effectiveness of PMT and expression of folate enzymes in lung cancer cells is unknown. The purpose of this study is to determine whether TS, DHFR, and GARFT expression affect therapeutic efficacy of PMT.

Methods: The subjects were advanced NSCLC patients who treated with PMT. Samples were gotten by tumour biopsy before treatment. We dissected cancer cells from formalin-fixed paraffin-embedded tissues by using a laser microdissection. TS, DHFR, and GARFT mRNA were analyzed by using real-time RT-PCR. We assessed the association between TS, DHFR, and GARFT mRNA expression and therapeutic efficacy of PMT.

Results: Twenty-nine patients were enrolled. The median age was 67 years. Seventy-two percent of patients had a previous treatment with chemotherapy. Overall response rates were 27.6% for PMT. Median progression free survival (PFS) was 22.5 weeks for PMT. TS mRNA levels ranged from 0.001 to 33.590 (mean 2.451). TS mRNA expression was significantly lower in response group (CR+PR) compared with non-response group (SD+PD) (0.223 ± 0.083 versus 3.195 ± 1.752, $p < 0.001$). DHFR and GARFT mRNA expression were not correlated with response rate. PFS was superior for lower DHFR and GARFT mRNA expression patients compared with higher DHFR and GARFT mRNA expression patients, which was not statistically significant. (DHFR 29.1 versus 16.6 weeks, $p = 0.158$, GARFT 30.7 versus 16.6 weeks, $p = 0.071$).

Conclusions: We could analyze TS, DHFR, and GARFT mRNA expression in lung cancer cells specifically from biopsy specimens by using a laser microdissection. TS mRNA expression affected therapeutic efficacy of PMT. TS mRNA expression may be usefull predictive biomarker for NSCLC patients received PMT.

9134 POSTER

Tumour Response, Skin Rash and Health-related Quality of Life (HRQoL) − Post-hoc Data From the IPASS Study

Y. Wu[1], M. Fukuoka[2], T.S.K. Mok[3], N. Saijo[2], S. Thongprasert[4], J.C.H. Yang[5], D.T. Chu[6], J.J. Yang[1], Y. Rukazenkov[7]. *[1]Guangdong General Hospital, Guangdong Lung Cancer Institute Guangdong Academy of Medical Sciences, Guangzhou, China; [2]Kinki University School of Medicine, Department of Oncology, Osaka-Sayama, Japan; [3]The Chinese University of Hong Kong, State Key Laboratory in Oncology in South China Sir YK Pao Center for Cancer Department of Clinical Oncology, Hong Kong, China; [4]Chiang Mai University, Faculty of Medicine Maharaj Nakorn ChiangMai Hospital, ChiangMai, Thailand; [5]National Taiwan University, National Taiwan University Hospital and College of Medicine, Taipei, Taiwan; [6]Chinese Academy of Medical Sciences, Cancer Institute and Hospital, Beijing, China; [7]AstraZeneca, Research and Development, Macclesfield, United Kingdom*

Background: IPASS (NCT00322452) demonstrated significantly longer progression-free survival (PFS) with first-line gefitinib *v* carboplatin/paclitaxel in never/light ex-smokers with advanced pulmonary adenocarcinoma in Asia, in the overall intent-to-treat (ITT) population and *EGFR* mutation-positive subgroup. We investigated objective response rate (ORR) and HRQoL in patients treated with gefitinib (ITT; *EGFR* mutation-positive subgroup) to further characterise the clinical relevance of the PFS data.

Methods: Objective response was assessed (RECIST) 6-weekly. Median time to response was summarised, median duration of response calculated (from first confirmed response visit) and change in tumour size assessed (percentage change from baseline) post-hoc. Patients without an end date were censored at their last evaluable assessment. The percentage of patients with a deterioration in HRQoL (reduction in Functional Assessment of Cancer Therapy-Lung [FACT-L; $\geqslant$6 points], Trial Outcome Index [TOI; $\geqslant$6 points]) or symptoms (Lung Cancer Subscale [LCS; $\geqslant$2 points]) at 4 months post-randomisation (median time on carboplatin/paclitaxel) was analysed according to progression status (post-hoc logistic regression adjusted for gender [male *v* female], WHO performance status [PS 0, 1 *v* 2] and smoking history [never *v* light ex-smoker]).