**9004** ORAL

**BRCA1 and Astrocyte Elevated Gene-1 (AEG-1) Expression and Outcome of Erlotinib-Treated Non-Small-Cell Lung Cancer (NSCLC) Patients (p) Harboring Epidermal Growth Factor Receptor (EGFR) Mutations**

M. Taron[1], S.B. Benlloch[2], J.J.S. Sanchez[3], R.R. Rosell[1], C.C. Costa[2], C.Q. Queralt[1], C.M. Mayo[2], I.A. de Aguirre[1], T.M. Moran[1], B.M. Massuti[4]. [1]*Catalan Institute of Oncology Hospital Universitari Germans Trias i Pujol, Oncology, Badalona (Barcelona),* [2]*Pangaea Biotech USP Dexeus University Institute, Oncology, Barcelona,* [3]*Autonomous University of Madrid, Statistics, Madrid,* [4]*Hospital General de Alicante, Oncology, Alicante, Spain*

**Background:** Progression-free survival (PFS) to erlotinib is 14 months (m) in EGFR-mutant NSCLC p. Aberrant expression of components of DNA repair pathways could shed light on the variability of PFS in these patients.
**Material and Methods:** We used the NanoString nCounter gene expression system, which captures and counts individual mRNA transcripts, to analyze the expression of 44 selected genes in 55 erlotinib-treated NSCLC p with EGFR mutations. Quantitative PCR was used to validate results in these 55 p and to confirm our findings in 22 additional p. Expression levels were correlated with clinical outcomes in all 77 p.
**Results:** We generated a two-gene risk model, classifying patients into low-, intermediate-, and high-risk groups, based on expression levels of both BRCA1 and AEG-1. PFS was not reached in the low-risk group, while it was 18 m for the intermediate-risk group and 8 m for the high-risk group ($P = 0.00006$) (HR for high- vs low-risk groups, 6.6; 95% CI, 2−4-18; $P < 0.00001$). MS was not reached in the low-risk group, while it was 31 m for the intermediate-risk group and 18 m for the high-risk group ($P = 0.05$). Complete response was attained in 42.9% of patients in the low-risk group, compared to 3% in the intermediate-risk group and 0% in the high-risk group ($P = 0.02$). In the multivariate analysis for PFS, the only independent prognostic variables were bone metastases (HR, 2.7; 95% CI, 1.1−6.5; $P = 0.03$) and the AEG-1/BRCA1 risk groups (HR for high-risk group, 7.7 (95% CI, 2.8–21.3; $P < 0.00001$).
**Conclusions:** The BRCA1/AEG-1 model provides robust predictive information, making it a useful tool for therapeutic decision making.

**9005** ORAL

**Is There a Benefit to Maintenance Therapy After First Line Chemotherapy in Advanced Non-small Cell Lung Cancer − a Systematic Review With Meta-analysis**

G. Des Guetz[1], B. Uzzan[2], K. Chouahnia[1], P. Nicolas[1], M. Perol[3], J.F. Morere[1]. [1]*Hopital Avicenne, Oncology, Bobigny,* [2]*Hopital Avicenne, Pharmacology, Bobigny,* [3]*Centre Léon Bérard, Pneumology, Lyon, France*

**Background:** Maintenance therapy refers to a treatment of extended duration after frontline induction chemotherapy (CT), for patients with advanced non-small cell lung cancer (NSCLC). Several recent randomized clinical trials (RCTs) showed a survival benefit for maintenance therapy, especially for EGFR tyrosine-kinase inhibitors (TKI), but conflicting results have been published. We performed a meta-analysis of all RCTs, published either as articles or as abstracts.
**Patients and Methods:** PubMed query using keywords simultaneously: Non Small cell Lung Cancer, Maintenance, Randomized Controlled trials, Survival found 70 references. Abstracts from ASCO and ESMO proceedings were also reviewed. Endpoints were Overall Survival (OS) and Progression Free Survival (PFS). We used a fixed-effect model when heterogeneity was absent and a random-effect model when present. We used EasyMA software.
We included 11 RCTs with IFCT-GFPC trial used twice since it studied 2 maintenance options, chemotherapy and Erlotinib (a TKI). These 11 RCTs included 4281 patients (mean age 61.7 years, 2907 men/1345 women, stage III/IV 1007/3206, adenocarcinoma/ squamous/other histology 2101/998/753, PS0/1/2 1600/2232/241, 2337 received active drugs).
**Results:** The 5 RCTs assesing a TKI found a statistically significant increase in PFS (HR 0.76; 0.62–0.93, $p = 0.007$) but not in OS (both using random-effect model due to heterogeneity with fixed-effect model). This benefit was higher when pooling only the 3 Erlotinib studies (HR OS 0.85, 0.76–0.95, $p = 0.003$; HR PFS 0.71, 0.64–0.79, $p = 0.001$, fixed-effect models).
Switch maintenance with CT (3 RCTs) significantly improved OS (HR 0.85, 0.75–0.98, $p = 0.02$) and PFS (HR 0.66, 0.57–0.76, $p = 0.001$). Continuation maintenance with CT (4 RCTs) did not improve OS (random-effect model). Side-effects were less precisely assessed by the authors in the RCTs. TKIs induced cutaneous rashes and diarrheas. As expected, all CT increased haematological side-effects.
**Conclusions:** Maintenance therapy, either TKI (erlotinib) or switch CT, significantly improved both OS and PFS. The benefits/risks balance of these 2 kinds of switch maintenance therapy should be compared.

**9006** ORAL

**Results of a Phase 2 Study of Gemcitabine/Cisplatin/Iniparib (GCI) Versus Gemcitabine/cisplatin (GC) in Patients With Advanced NSCLC**

S. Novello[1], E. Felip[2], F. Barlesi[3], J. Mazieres[4], G. Zalcman[5], J. von Pawel[6], M. Reck[7], F. Cappuzzo[8], D. Ferry[9], J.C. Soria[10]. [1]*University of Torino, Thoracic Oncology Unit − San Luigi Hospital, Torino, Italy;* [2]*Vall d'Hebron University Hospital, Medical Oncology Service, Barcelona, Spain;* [3]*Université de la Méditerranée-Assistance Publique Hôpitaux de Marseille, Department of Thoracic Oncology, Marseille,* [4]*Hôpital Larrey, Service de Pneumologie, Toulouse,* [5]*CHU Côte de Nacre, Service de Pneumologie, Caen, France;* [6]*Asklepios-Fachkliniken Munchen-Gauting, Klinik fur Pneumologie, Gauting,* [7]*Hospital Grosshansdorf, Department of Thoracic Oncology, Grosshansdorf, Germany;* [8]*Ospedale Civile di Livorno, Division of Medical Oncology, Livorno, Italy;* [9]*New Cross Hospital, Department of Oncology, Wolverhampton, United Kingdom;* [10]*Institut Gustave Roussy, Department of Medicine, Villejuif, France*

**Background:** Iniparib (BSI-201) is a novel agent being studied in combination with chemotherapeutic agents in a range of solid tumours. At high μM concentrations, iniparib binds to PARP1; however, the mechanism of action is not fully understood and is under investigation. Iniparib combined with gemcitabine/carboplatin (GCI) improved efficacy outcomes in a Phase 2 study in patients (pts) with metastatic triple-negative breast cancer with no increase in toxicity; however, an OS benefit was not confirmed in the Phase 3 setting. The present randomised, open label Phase 2 study will be the first completed efficacy trial in NSCLC of iniparib in combination with GC as first-line therapy (Clinicaltrials.gov number NCT01086254).
**Methods:** Eligible pts ($n = 119$) had histologically confirmed stage IV NSCLC, without prior chemotherapy for stage IV disease. Pts were randomised (2:1) to receive G (1250 mg/m$^2$, IV; d 1, 8), and C (75 mg/m$^2$, IV; d 1) (GC), ± iniparib (5.6 mg/kg, IV; d 1, 4, 8, 11; GCI) every 21 days for a maximum of 6 cycles. The primary objective was investigator assessed overall response rate. Secondary objectives were to assess OS, PFS, safety and biomarker utility. Randomisation was stratified by tumour histology (squamous/non-squamous) and smoking status.
**Results:** Pts received GCI (77 treated) or GC (39 treated). Median age was 59 years (29–73); 76% male; 12% of pts had squamous cell carcinoma and 70% adenocarcinoma; 13 (11%) were never-smokers. ECOG PS 0 vs.1 was 49 vs. 51% and 61 vs. 39% in the GC/GCI arms, respectively. As of December 2010, >60% of pts were still receiving treatment. Dose reductions, dose intensity, number of cycles (median 3), and discontinuations due to tumour progression or adverse events were similar in both arms. The safety profile was similar in both arms; however, more pts in the GC arm required dose reductions due to neutropenia (23.1 vs. 10.4%). Febrile neutropenia was only reported in the GC arm ($n = 2$). Rates of thrombocytopenia were similar in the GC/GCI arms (10.3 vs. 9.1%, all grades); asthenia was more frequent in the GC vs. GCI arm (66.7 vs. 46.8%, all grades; 15.4 vs. 4.9%, Grade 3/4). Neurotoxicity (all grades) was more frequent in the GC arm, with no Grade 3/4 events.
**Conclusions:** In pts with metastatic NSCLC, combination therapy with GCI had a similar safety profile to that seen with standard doses of GC, with no additional toxicities. Final efficacy and safety data will be presented.

**9007** ORAL

**Phase II Study of Afatinib (BIBW 2992), an Irreversible ErbB Family Blocker, in Patients With EGFR FISH-positive Advanced NSCLC**

G. Finocchiaro[1], A. Santoro[1], F. Grossi[2], P. Bidoli[3], A. Favaretto[4], L. Clementi[5], D. Massey[5], R. Lorence[6], F. Cappuzzo[7]. [1]*Humanitas Cancer Center, Cancer Center, Rozzano,* [2]*National Institute for Cancer Research, Cancer Research, Genova,* [3]*S. Gerardo Hospital, Oncology, Monza,* [4]*Hospital of Padova, Oncology, Padova,* [5]*Boehringer Ingelheim Italia S.p.A., Italia S.p.A., Milan, Italy;* [6]*Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield CT, Oncology, USA;* [7]*Livorno Hospital, Oncology, Livorno, Italy*

**Background:** Afatinib (A), a potent irreversible tyrosine kinase inhibitor (TKI) of the erbB family of receptors, has previously shown high activity in NSCLC patients (pts) harboring EGFR mutations (Yang et al., ESMO 2010, Abstract 367PD). However, it is not known if this activity extends to those pts with increased EGFR gene copy number (GCN). We conducted a multicenter Phase II study to evaluate efficacy of A in pts with advanced NSCLC and increased EGFR GCN identified by FISH testing.