43% and 44% of pts receiving AMR or Topo, respectively, and 4 AMR pts (5%) died of neutropenic infection. Changes in LVEF from BL were minimal even in 13 pts who received cumulative AMR doses >1000 mg/m^2.
Conclusion: AMR significantly improves ORR vs Topo and has acceptable tolerability as 2nd-line therapy in pts with sensitive ED-SCLC. AMR has an improved early cardiac safety profile relative to other anthracyclines, but long-term effects are unknown.

9121 POSTER

Amrubicin monotherapy in patients with extensive disease small cell lung cancer (ED-SCLC) refractory to first-line platinum-based chemotherapy: final results of a phase 2 trial

D.S. Ettinger[1], R. Jotte[2], P. Lorigan[3], V. Gupta[4], L. Garbo[5], D. Spigel[6], A.Z. Dudek[7], R. Salgia[8], R. McNally[9], M. Renschler[10]. *[1]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Medical Oncology, Baltimore, USA; [2]Rocky Mountain Cancer Centers US Oncology, Medical Oncology, Denver, USA; [3]Christie Hospital NHS Foundation Trust, Medical Oncology, Manchester, United Kingdom; [4]St Joseph Oncology US Oncology, Medical Oncology, St. Joseph, USA; [5]New York Oncology Hematology US Oncology, Medical Oncology, Albany, USA; [6]Sarah Cannon Cancer Center, Medical Oncology, Nashville, USA; [7]Masonic Cancer Center University of Minnesota, Medical Oncology, Minneapolis, USA; [8]University of Chicago, Medical Oncology, Chicago, USA; [9]Celgene Corporation, Biostatistics, Summit, USA; [10]Celgene Corporation, Clinical Development, Summit, USA*

Background: Amrubicin (AMR) is a 3rd-generation synthetic anthracycline and potent topoisomerase II inhibitor. It is approved in Japan for treatment of NSCLC and SCLC. Literature indicates that SCLC patients (pts) who are refractory to 1st-line chemotherapy are unlikely to respond to additional chemotherapy and their expected median survival is 3−5 mos. This phase 2 open-label trial (NCT 00375193) evaluated the efficacy and safety of AMR monotherapy for treatment of pts with refractory ED-SCLC.
Methods: Pts with ED-SCLC refractory to 1st-line platinum-based chemotherapy (progression [PD] during therapy or relapse $\leqslant$90 days of treatment end) and ECOG performance status (PS) $\leqslant$2 were eligible. Pts received IV AMR 40 mg/m^2/day $\times$3 days every 21 days until PD, unacceptable toxicity, or withdrawal. The primary endpoint was overall response rate (ORR, CR+PR; by RECIST), with a goal of demonstrating an ORR $\geqslant$18%. Secondary endpoints included time to progression (TTP) duration of response (DR), progression-free survival (PFS) and overall survival (OS). Left ventricular ejection fraction (LVEF) was measured by ECHO or by MUGA at baseline, cycles 3, 6, then every 2 cycles, and end of treatment.
Results: 75 patients enrolled; median age was 63 years (range 43−88) and 17% were PS 2. Median time from end of 1st-line therapy to PD was 1.3 mos. Six pts died or discontinued before receiving AMR; the remaining 69 pts (92%) received a median of 4 AMR cycles (range 1−12). The primary endpoint was met: ORR was 21% (16/75, 95%Clopper-Pearson lower bound 13.9%), including 1 CR (1%) and 15 PR (20%). Stable disease (SD) was achieved by 30 (40%) pts. Of note, 7 pts with SD or PD as best response to 1st-line therapy achieved a PR with AMR treatment. Median DR was 4.3 months (95% CI 3.1, 5.8 mos), TTP was 3.8 mos (95% CI 2.7, 4.2 mos), PFS was 3.3 mos (95% CI 2.5, 4.0 mos), and OS was 6.1 mos (95% CI 4.9, 7.2 mos). Changes from baseline LVEF were similar across cumulative dosing groups, including in 4 pts who received cumulative AMR doses >1000 mg/m^2. The most common grade 3 or 4 adverse events were neutropenia (67%), thrombocytopenia (41%), and leukopenia (35%). Eight pts (12%) experienced febrile neutropenia. Twenty-six pts (38%) required dose reductions.
Conclusions: AMR shows promising activity in pts with refractory ED-SCLC, with an ORR of 21% and an acceptable safety profile.

9122 POSTER

Phase I study with pemetrexed, cisplatin and concurrent radiotherapy in limited-stage small cell lung cancer (LS-SCLC)

V. Surmont[1], K. Nackaerts[2], S. Senan[3], C.J. Kraaij[4], N. Chouaki[5], R.J. van Klaveren[6], J. Vansteenkiste[7], E.F. Smit[8]. *[1]UZ Gent, Respiratory Medicine/Thoracic Oncology, Gent, Belgium; [2]University Hospital Gasthuisberg Leuven, Pulmonology, Leuven, Belgium; [3]Vrije Universiteit Medical Center, Radiation Oncology, Amsterdam, The Netherlands; [4]Eli Lilly, Oncology, Houten, The Netherlands; [5]Eli Lilly, Radiation Oncology, Paris, France; [6]Erasmus Medical Center/Daniel den Hoed Cancer Clinic, Thoracic Oncology, Rotterdam, The Netherlands; [7]University Hospital Gasthuisberg, Pulmonology, Leuven, Belgium; [8]Vrije Universiteit Medical Center, Pulmonology, Amsterdam, The Netherlands*

Background: The activity of the combination of pemetrexed and cisplatin (P/Cis) in extensive stage (ES) SCLC (Socinski et al, JCO 2006) coupled with its radiosensitizing properties provided the rationale for this study. The study was stopped early based on interim results of the GALES trial in December 2007, showing inferior activity of P/carboplatin compared to etoposide/carboplatin in ES-SCLC.
Materials and Methods: Treatment-naïve patients (pts) with a diagnosis of LS-SCLC, without cytologically-proven malignant pleural effusion, were entered. This was an open-label, dose-escalation study, with 3−6 pts to be treated in each of the 4 planned cohorts (Coh): escalating pemetrexed doses (400−500 mg/m^2) and 75 mg/m^2 Cis administered intravenously for four 21-day cycles, concurrent with thoracic radiotherapy (TRT) 50 to 62 Gy starting at cycle 2. Endpoints were determination of recommended dose, maximum tolerated dose (MTD), dose-limiting-toxicity (DLT), acute and late toxicities and best overall response.
Results: A total of 9 pts were entered, age 50−80 years, 6 male, 3 female, 2 with ECOG performance status (PS) 0 and 7 with PS 1. The study was stopped too early to assess recommended dose or MTD. Three pts in Coh 2 discontinued due to adverse events after 1 or 2 treatment cycles (renal failure, femoral artery occlusion, peripheral sensory neuropathy). There was no DLT during TRT up to 6 weeks after treatment, 3 Coh 2 pts were replaced as they were not evaluable for DLT. Four pts experienced at least one possibly drug-related serious adverse event: one in Coh 1 (oesophagitis grade 2, anaemia grade 3, diverticulitis, malaise) and three in Coh 2 (sensory neuropathy grade 3, nausea, fatigue, anorexia, dehydration, femoral artery occlusion). One patient experienced oesophagitis grade 3 but was able to complete treatment without delay in TRT. There was no febrile neutropenia and no toxic death.

The most common (>1) related CTC grade 3/4 toxicities

CTCAE grade 3/4	Cohort 1 P 400 mg/m^2* (N = 3)	Cohort 2 P 500 mg/m^2* (N = 6)
Anorexia	2	1
Lymphopenia	1	2
Dehydration	1	1
Neutropenia	1	1
Thrombocytopenia	2	0

*plus 75 mg/m^2 Cis, 50 Gy TRT

The best overall response in Coh 1 was 2 partial responses (PR), 1 progressive disease (PD) and in Coh 2 was 1 PR.
Conclusions: Although the recommended dose of P/Cis and TRT could not be assessed, these data show that the combination of systemic doses of 75 mg/m^2 Cis and 500 mg/m^2 P concurrent with 50 Gy TRT is well tolerated. Pemetrexed is the first 3rd generation cytotoxic found to be tolerable at full dose with concurrent radiotherapy.

9123 POSTER

Screening of lung carcinoids for somatic mutations of MEN1 gene

S. Veschi[1], G. Aceto[1], S. Magnasco[2], R. Lattanzio[3], M.C. Curia[3], D. Angelucci[2], R. Mariani-Costantini[3], P. Battista[1]. *[1]University "G. d' Annunzio", Department of Human Movement Sciences, Chieti Scalo, Italy; [2]"S.S. Annunziata" Hospital, Institute for Pathological Anatomy, Chieti Scalo, Italy; [3]Center for Sciences on the Ageing (CeSI) "G. d'Annunzio" University Foundation and University "G. d'Annunzio", Department of Oncology and Neurosciences, Chieti Scalo, Italy*

Background: Pulmonary carcinoids (PC), that occur sporadically and rarely in association with multiple endocrine neoplasia type 1 (MEN1) are relatively rare neoplasms that express neuroendocrine markers