

non-adherence in 23/63 (36.5 %) and good adherence in 29/63 (46%). Agreement between clinician assessment and prescription issue data were seen in only 23/63 (36.5%) of cases and overall agreement using a weighted  $\kappa$  coefficient was poor (weighted agreement 63.5%, expected agreement 58.8%,  $\kappa$  0.11, SE 0.1,  $z=1.16$ ,  $p=0.12$ ). There was no relationship between patients' age, gender, Juniper asthma control score, prescribed inhaled corticosteroid dose or FEV<sub>1</sub> percent predicted and the chances of agreement or disagreement between the two methods.

**Conclusions** Clinical judgement alone appears to be a poor predictor of adherence to medication in patients with difficult asthma. The assessment of non-adherence requires objective measurements. Prescription issue data are one such measurement; but further work is required.

## Lung cancer: advances in treatment

**S85** **BRITISH THORACIC ONCOLOGY GROUP TRIAL, BTOG2: RANDOMISED PHASE III CLINICAL TRIAL OF GEMCITABINE COMBINED WITH CISPLATIN 50 MG/M<sup>2</sup> (GC50) VS CISPLATIN 80 MG/M<sup>2</sup> (GC80) VS CARBOPLATIN AUC 6 (GCB6) IN ADVANCED NSCLC**

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**Background** Platins are considered key drugs in treating advanced NSCLC. Carboplatin has been reported as inferior to cisplatin in meta-analyses while the optimal dose of cisplatin is unclear.

**Methods** Eligibility was by histologically proven NSCLC, PS 0–2, stage IIIB/IV disease and a GFR of >60 ml/min, using the Wright equation. Treatment was gemcitabine (1250 mg/m<sup>2</sup>) combined with cisplatin 50 mg/m<sup>2</sup>, cisplatin 80 mg/m<sup>2</sup> or carboplatin AUC 6, for up to four cycles. Carboplatin dosing was calculated using the Calvert equation. At the time of analysis 1223 deaths had been reported, allowing analysis according to the statistical plan.

**Results** 1363 patients were randomised between April 2005 and November 2009. Trial arms were well balanced for PS, stage and age. Median age was 63, 32% were PS0, 60% PS1 and 8% PS2. The median delivered dose intensities (planned=100%) for platinum were GC50 99%, GC80 96% and GCB6 87%, for gemcitabine were 95%, 88% and 80% respectively. During treatment the proportion of patients experiencing at least one grade 3/4 AE were; GC50 27%, GC80 41% and GCB6 57%. At analysis 140 patients were alive and median follow-up was 21 months. Response rates were significantly different between arms; GC50 23%, GC80 33% and GCB6 28% ( $p=0.01$ ). Median survival was: GC50 8.3 months, GC80 9.5 months and GCB6 10.0 months, with the GC50 arm statistically identified as differing from the other two. For subsequent primary comparisons of non-inferiority of GC50 v GC80 (HR=1.11) and GCB6 v GC80 (HR=0.96), the 95% CI for the cisplatin dose comparison (0.96, 1.27) did not exclude the pre-defined inferiority region of HR>1.2 whereas the 95% CI for the GCB6 v GC80 comparison (0.84, 1.10) fell well below this inferiority region.

**Conclusion** In advanced NSCLC the dose of cisplatin is important with GC50 giving the poorest outcome in terms of overall survival and response rate. GCB6 is not inferior to GC80 thus, in combination with gemcitabine, and in relation to survival time, carboplatin is

clinically equivalent to that of cisplatin but other factors, such as quality of life, may influence treatment choice.

**S86** **QUALITY OF LIFE IN ADVANCED NON-SMALL CELL LUNG CANCER, EFFECTS OF CISPLATIN DOSE AND CARBOPLATIN IN COMBINATION WITH GEMCITABINE: RESULTS FROM BTOG2, A BRITISH THORACIC ONCOLOGY GROUP PHASE III TRIAL IN 1363 PATIENTS**

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**Background** The standard of care for advanced NSCLC is platinum-based chemotherapy but the optimal dose of cisplatin and comparison with carboplatin is uncertain. With median survival at 8–12 months, the impact of such treatment choices on patients' quality of life (QoL) is important. The BTOG2 trial is a large phase III randomised trial comparing three treatment arms: gemcitabine (1250 mg/m<sup>2</sup> day 1 and day 8) with either cisplatin 80 mg/m<sup>2</sup> (GC80), cisplatin 50 mg/m<sup>2</sup> (GC50) or carboplatin AUC6 (GCB6). The trial was innovative in aiming to collect QoL data on all trial patients and is the largest study to date addressing this issue in NSCLC.

**Methods** QoL was measured at each cycle of chemotherapy and each follow-up visit using standard, validated questionnaires: EORTC QLQ-C30, LC13 and EQ-5D.

**Results** More than 8000 questionnaires were returned from 1363 randomised patients with compliance around 90% during the treatment period. At pre-randomisation, the mean global health status score and EQ-5D utility score were 62% and 0.66. On initiation of treatment, patients in all three treatment arms had improved pain, cough, haemoptysis, insomnia, appetite loss and emotional functioning with associated improvements in global measures of QoL but these benefits generally fell away after completion of chemotherapy (12+ weeks). GC50 performed better in terms of the functioning scores and in terms of fatigue, nausea and vomiting while GCB6 performed worst for dyspnoea. All treatments had a deleterious effect on peripheral neuropathy with the post-treatment toxicity momentum markedly worse for GC80. Mean quality-adjusted life months were 6.1 on GC80, 5.6 on GC50 and 6.1 on GCB6.

**Conclusion** Although higher doses of cisplatin (80 mg/m<sup>2</sup>) are thought detrimental to QoL compared to 50 mg/m<sup>2</sup> we found minimal differences but a noteworthy problem in delayed neuropathy. Also, the belief that carboplatin produces superior QoL compared to cisplatin at either dose is not obvious. Importantly carboplatin treatment may not palliate dyspnoea as well as cisplatin. Adjusting for QoL does not change the conclusions from the primary survival analysis.

**S87** **DELIVERED DOSE INTENSITY OF GEMCITABINE 1250 MG/M<sup>2</sup> WITH CISPLATIN AT 80 MG/M<sup>2</sup> (GC80) AND 50 MG/M<sup>2</sup> (GC50) AND CARBOPLATIN AUC 6 (GCB6) IN A PHASE III TRIAL OF ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC): CORRELATIONS WITH CLINICAL OUTCOMES**

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**Background** Chemotherapy agents have dose-related effectiveness. The BTOG2 trial is a large phase III trial supported by the British Thoracic Oncology Group patients addressing this issue in which advanced non-small cell lung cancer were randomised to GC80 vs GC50 vs GCb6. Treatment delays and dose reductions due to toxicity mean that patients do not actually receive planned treatments and the BTOG2 trial provides an opportunity to investigate the delivered dose intensity (DDI) of these treatments in a large group of patients.

**Methods** Carboplatin dose was calculated using the Calvert equation, incorporating estimated GFR based on the Wright equation including creatinine kinase. Delivered dose intensity (DDI) for each patient was calculated as the mean of the per-cycle DDI which is the ratio of the delivered vs planned dose per day, calculated for platinum and gemcitabine separately.

**Results** Starting doses for cycle 1 were generally as per protocol. Doses of carboplatin are higher using estimated GFR from the novel Wright formula compared to standard Cockcroft–Gault approach. Dose reductions on cycles 2–4 were more apparent for GC80 compared to GC50 (56% vs 42% with =1 dose reduction) but dose delivered remained high with reductions to median of 77 mg/m<sup>2</sup> by cycle 4. Dose reduction rate was highest on GCb6 with 71% of patients experiencing =1 reduction, with median dose of AUC 4.5 at cycle 4. Gemcitabine dose reductions paralleled those seen with platinum, occurring more frequently with GCb6. Overall DDI for platinum was high for all treatments but lowest for GCb6 (96% vs 99% vs 87%). Response rates were GC50 23%, GC80 33% and GCb6 28%. There was no evidence that dose reductions, treatment delays or DDI was associated with response thus the delivered dose of GC80 was sufficient to generate this 10% difference.

**Conclusion** Doses of cisplatin at 80 mg/m<sup>2</sup> and carboplatin at AUC6 based on the Wright formula in combination with gemcitabine are deliverable but individuals have higher chance of treatment delays and dose reductions with carboplatin. However the reduced DDI does not appear to have an effect on clinical outcomes.

#### S88 DAY CASE CISPLATIN DELIVERY FOR ADVANCED NSCLC PATIENTS: FASTER, CHEAPER, MORE DESIRABLE

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**Background** The BTOG2 trial was a phase III randomised clinical trial in the treatment of advanced NSCLC. It investigated the optimal dose of cisplatin (50 vs 80 mg/m<sup>2</sup> 3-weekly), in combination with gemcitabine, and whether carboplatin (AUC6-Wright) could safely and effectively be substituted for the optimal cisplatin

dose. The protocol recommended cisplatin given as an out-patient regimen designed to ensure diuresis while maintaining electrolytic balance. A previously reported audit by these authors, 48% of hospitals surveyed were admitting NSCLC patients for cisplatin /gemcitabine chemotherapy.

**Methods** Between April 2005 and November 2009, 909 patients were randomised to receive cisplatin, in the UK and Ireland, as part of BTOG2. The trial mandated submission of proposed chemotherapy delivery schedules to ensure standard parameters in terms of: total duration of delivery, mandatory use of mannitol, short 1-h delivery of cisplatin and total fluid volume <4 l. Data mining was used to investigate AEs relating to renal function, electrolyte imbalance and ototoxicity. AEs that could feasibly be related to the manner in which cisplatin was administered.

**Results** 2853 treatment cycles were available for analysis. Average treatment duration decreased from nearly 9 to 6 h and total fluid volume from as much as 7 to <4 l. As a result of participating in BTOG2, 97% of surveyed hospitals were able to deliver cisplatin in a day case setting. Toxicities feasibly related to the manner in which cisplatin was administered were comparable to the current available literature with <1% experiencing grade >2.

**Conclusion** Current NHS Tariffs in the UK quote a 60% higher price for patients being inpatient cisplatin treatment as opposed to outpatient. With the prima facie case that patients prefer outpatient treatment, it is important to achieve the maximum benefit from the existing drugs in a clinically deliverable way. The results indicate that administering cisplatin via a short hydration schedule of <6 h, even at 80 mg/m<sup>2</sup>, is safe. It is unlikely that the many hospitals who changed their practice would have done so without the support of a running randomised controlled trial.

#### S89 A META-ANALYSIS OF LIMITED RESECTION VS LOBECTOMY FOR STAGE I NON-SMALL CELL LUNG CANCER

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#### WITHDRAWN

#### S90 NURSE SPECIALIST INPUT IS INDEPENDENTLY ASSOCIATED WITH ANTI-CANCER TREATMENT IN LUNG CANCER

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**Introduction** Lung cancer nurse specialists (LCNS) provide an extremely important service to patients. Their skill and expertise are valued very highly by both patients and colleagues, but it has proven difficult to measure their input objectively, leading to a lack of expansion (and in some areas contraction) of the workforce. Earlier this year the National Lung Cancer Audit (NLCA) reported that for 2009, patients who saw an LCNS were more than twice as likely to

Abstract S90 Table 1

	Number having treatment (%)		OR (95% CI) vs no nurse/unknown	
	Seen by nurse	Not seen by nurse/unknown	All patients	Patients surviving >28 days
Anti-cancer treatment	14 631 (64.5%)	3080 (40.4%)	2.04 (1.91 to 2.18)	1.87 (1.74 to 2.01)
Surgery	3456 (15.3%)	922 (12.1%)	1.06 (0.97 to 1.17)	1.01 (0.91 to 1.11)
Chemotherapy	7708 (34.0%)	1247 (16.4%)	2.05 (1.90 to 1.22)	1.87 (1.72 to 2.02)
Radiotherapy	7140 (31.5%)	1474 (19.3%)	1.57 (1.47 to 1.68)	1.47 (1.38 to 1.59)