Methods: In protocol 9801, 401 pts with BM from any primary tumor were randomized to receive WBRT alone (30 Gy/10 fractions) or MGd, 5 mg/kg qd x 10 days, with WBRT. The subgroup of 251 pts with NSCLC is included in this analysis. In protocol 0211, 554 pts with BM from NSCLC were randomized to the same treatments. In both studies, eligibility included a KPS ≥ 70, no liver metastases, and ≤ 1 site of extracranial metastasis. In both studies, patients underwent a battery of neurocognitive tests measuring memory and executive function at baseline and all subsequent monthly follow-up visits. Progressions were defined as a confirmed decline from baseline of 1.5 standard deviations, corrected for age and educational background.

Results: 805 pts received WBRT (N=403) or MGd+WBRT (N=402). Most pts had multiple BM (81%), extracranial metastases (47%) and presented with neurologic deficits (84%). Treatment arms were balanced for key prognostic factors. At baseline, 77% of all patients had some degree of neurocognitive deficit with 18% having one test result abnormal, 20% having two, 18% having three, 16% having four and 5% having all five results abnormal. Memory was the most frequently impaired function (57%). Baseline neurocognitive impairments were balanced across treatment arms. Patients treated with MGd+WBRT were less likely during follow-up to show evidence of neurocognitive progression in memory function (HR=0.80, p=0.047), in executive function (HR=0.74, p=0.028) or in a combined score for all tests, (HR=0.78, p=0.02).

Conclusions: Consistent with the delay in time to clinical neurocognitive progression seen in a previous pooled analysis, treatment with MGd+WBRT decreased progression in each function measured by standardized neurocognitive testing in the pooled dataset from 2 randomized phase III trials.

Session B2: Cytotoxic Chemotherapy II
Tuesday, September 4

B2-01 Cytotoxic Chemotherapy II, Tue, 13:45 - 15:30

The NATCH trial: chemotherapy toxicity and response on the neoadjuvant arm
Felip, Enrique1a Rosell, Rafael2 Massuti, Bartomeu3 Alonso, Guillermo4 Gonzalez-Larriba, Jose-Luis5 Camps, Carlos6 Isla, Dolores7 Mas, Cristina8 Sanchez, Jose Javier9 Maestre, Jose Antonio9

1 Vall d’Hebron University Hospital, Barcelona, Spain 2 Hospital Germans Trias i Pujol, Badalona, Spain 3 Hospital General Universitario de Alicante, Alicante, Spain 4 Hospital Juan Canalejo, La Coruña, Spain 5 Hospital Clínico San Carlos, Madrid, Spain 6 Hospital General de Valencia, Valencia, Spain 7 Hospital Clínico Lozano Blesa, Zaragoza, Spain 8 Universidad Autonoma de Madrid, Madrid, Spain 9 Hospital Vall d’Hebron, Barcelona, Spain

Background: In early stage NSCLC, neoadjuvant chemotherapy is a promising option, although conclusive evidence is yet to be supplied. The NATCH trial was designed in order to address whether neoadjuvant or adjuvant paclitaxel(P)/carboplatin(C) improves disease-free survival compared to surgery alone in early-stage NSCLC. Analyses of toxicity, response rate, resectability rate and surgical mortality rates have now been carried out on patients randomized to the neoadjuvant arm.

Methods: Clinical stage I (> 2 cm), II, T3N1 NSCLC consenting patients are randomized to surgery alone or 3 cycles of neoadjuvant PC (P:200 mg/m2 C AUC:6 on day 1 every 3wk), or surgery followed by 3 cycles of adjuvant PC at the same schedule. This prospective, randomized trial planned to include 624 patients.

Results: Between April 2000 and March 2007, 623 patients have been accrued, 201 on the neoadjuvant arm; 211 on the adjuvant arm and 211 on the surgery arm. On the neoadjuvant arm, demographic data is now available for 162 patients: 89% male; median age 64 years (range, 37-78); 45% PS 0; 53% squamous cell, 27% adenocarcinoma, 13% large cell; 7% stage IA, 64% IB, 2% IIA, 24% IIB, 2.5% T3N1. To date, neoadjuvant chemotherapy has been well tolerated. No unexpected toxicities have been seen with 12% of patients having grade 3-4 neutropenia and 43% grade 1-2 anemia. Major radiographic response has been observed in 59% of patients and progression during chemotherapy occurred in 6%. No patient characteristics were predictive for clinical response. At thoracotomy resection procedures were: lobectomy or bilobectomy in 70%; pneumonectomy in 26%; and explorative thoracotomy due to unresectable disease in 3% of patients. Thirty-day post-operative mortality was 4%. At surgery, 9% patients had pathologic complete response; 75% N0-1 disease (with persistent T tumor), and 15% had pathologic N2 disease.

Conclusion: Our findings suggest that neoadjuvant chemotherapy in early NSCLC is feasible with manageable toxicity and with good resectability rates. Mature survival results of the NATCH trial are expected in 2009.