Background: Cetuximab (C225) is a chimerized monoclonal antibody that targets the epidermal growth factor receptor (EGFR). NSCLC commonly expresses the EGFR, which is associated with aggressive tumor behavior and poor clinical outcome. Preclinical model systems demonstrate radiosensitization following molecular inhibition of EGFR signaling. An ongoing Phase II trial is testing cetuximab, with CRT, in unresectable stage III NSCLC.

Methods: Eligibility criteria include Zubrod performance status (PS) ≤1, weight loss ≤5% over past 3 months, FEV1 ≥1.0 L, adequate hematologic, hepatic, and renal function. Patients start an initial dose of C225 (400 mg/m²) on day 1 of week 1, then receive weekly doses of C225 (250 mg/m²) until completion of therapy (weeks 2-17). During week 2, patients receive CRT (63 Gy/35 fractions) with weekly carboplatin (C) AUC 2 and paclitaxel (P) 45 mg/m² x 6 doses followed by C (AUC 6) and P (200 mg/m²) X 2 cycles (weeks 12-17). Interim monitoring for severe (grade ≥3) or excessive non-hematological toxicities will occur after CRT. Patients have been treated and followed for at least 90 days after CRT. Endpoints include safety and compliance of concurrent C225 and CRT.

Results: 41 patients have been entered to date with toxicity data available on 22. Pts characteristics (n = 33): 67% females, median age 68 years (range 42-84), 48% PS 0, 48% stage IIIA. Data on adverse events related to CRT (n = 22): 1 pt with grade 3 thrombocytopenia, 5 pts with grade 3 leukopenia and 1 pt with grade 4 leukopenia. Number of grade 3 non-hematological toxicities: Metabololabo (4), fatigue (4), pulmonary (2), dermatologic (1), anorexia (1), pain (1), and allergy (1). There have been no grade 4 non-hematological toxicities.

Conclusions: Patient accrual is ongoing. This regimen appears to be well tolerated. Updated toxicity will be reported.

Background: The disappointing results of surgical therapy in patients with locally advanced non small cell lung cancer (NSCLC) have led to the investigation of induction treatments. Of those, phase II trials studies have shown that chemoradiotherapy administered before surgery yields a downstaging with a significant complete pathologic response amount. These results are often linked to enhanced surgical toxicities and impact on survival is not clear.

The aim of this study was to assess the efficacy and morbidity of a novel chemo-radiotherapy regimen followed by surgery in patients with locally advanced NSCLC.

Methods: From October 2000 to October 2004, 92 patients (age 34-78 y, median 59 y, PS 0-1) with locally advanced NSCLC (12 IIIA, 22 IIIA, 47 IIIB, 11 IV) were proposed induction chemoradiotherapy. Chemotherapy consisted of 3 cycles of cisplatin 80-100 mg/m² + ifosfamide 3-4.5 g/m² + vinorelbine 25 mg/m² (32) and was administrated on days 1-2-8-15 (1 cycle) 29-30-36-43 (2nd cycle) and daily from day 56 to 64 (3rd cycle). Concurrent thoracic irradiation (40 Gy) was given from day 36 to 64. Three-dimensional dosimetry was performed using CT scan and ISIS treatment planning.

At the end of the induction treatment, 37 (initial staging: 9 IIIB, 12 IIIA, 14 IIIB, 2 IV) of these 92 patients (40%) demonstrated objective clinical downstaging, had a good general status and were submitted to surgical resection (lobectomy: 16, pneumonectomy 15 left and 8 right). For those 37 patients, median (SD) planning treatment volume was 656 (368) cm³, V20 and V30 were ≤7 (5) and (4.8), respectively. Mean (SD) fraction of oesophageal and heart receiving 49 Gy were 14 (18) and 14 (13) %, respectively.

Results: Complete pathological response was found in 12/37 patients (32%). Median follow-up of these 37 patients was 14 months (3-51) and projected 2 years survival is 66%. Main side effects of induction treatment included grade ≥3 oesophagitis and febrile neutropenia in 50 and 12% of the patients, respectively. The patients (all live but none with complete from AHSO. 2 early after massive haemorrhage and transfusion and 1 at day 15 without bleeding or infection. Otherwise, no infection or bronchopleural fistula was noted.

Conclusions: This preliminary study demonstrates that induction chemotherapy with cisplatin, ifosfamide, vinorelbine combined with thoracic irradiation can convert 40% of inoperable locally advanced NSCLC patients to candidates for surgical resection. Early results promise improvement in survival with high but tolerable toxicity.

Background: To test efficacy of a weekly schedule of paclitaxel and carboplatin in combination with hyperfractionated/accelerated radiotherapy (HF-XRT) in the neoadjuvant setting in locally advanced NSCLC.

Methods: Patients (≥17 to <70 years, KPS ≥70) with stage III NSCLC (staging: CT/bronch/diabrom/orison, PET, and mediastinoscopy) without supradiaphragmatic lymph node involvement were qualified for the study. Paclitaxel 100 mg/m² and carboplatin AUC 2 were administered at day 1, 8, 15, and 22 following HF-XRT starting at day 1 (2 x 1.5 Gy/day, 5x/week from day 45 to 49) with concurrent paclitaxel (50 mg/m²) and carboplatin (AUC 2) at day 44, 51, and 58. After complete restaging, resections were planned 4-6 weeks after completion of the neoadjuvant therapy.

Results: 120 patients have been entered and complete data are available (30 IIIA, 84 IIIB, 2 IV). Grade III and IV toxicity occurred in 40 and 4 patients, respectively. Significant downstaging, no change, and progressive disease was observed in 60%, 34%, and 6% of the cases. R0 resections could be achieved in 62% (52%) patients 15 (29%) patients had postoperative complete remission of the primary tumor and 31 (26%) patients complete remission of mediastinal nodes. After a median follow-up of 41 months, 81 relapses have been observed. Median survival was 14 months, 5 years overall survival was 29 months and 5 years overall survival was 84 months and 56% in complete resected patients and 9 months 0% in unresected patients (p < 0.0001).

Conclusions: In conclusion the tested neoadjuvant regimen exhibits tolerable toxicity, considerable activity and a promising 5 year survival of 56% for complete resected patients in advanced stage III lung cancer.