# Long-Term Results of a Phase II Trial of Induction Paclitaxel-Carboplatin Followed by Concurrent Radiation Therapy and Weekly Paclitaxel and Consolidation Paclitaxel-Carboplatin in Stage III Non-small Cell Lung Cancer

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**Introduction:** Long-term results of a phase II study on the use of induction chemotherapy (CHT) using paclitaxel (P)-carboplatin (C) followed by a concurrent radiation therapy (RT) and weekly P and consolidation PC were reviewed.

**Patients and Methods:** Thirty-two patients with stage III non-small cell lung cancer started treatment with induction CHT (two cycles of P 175 mg/m$^2$, day 1 and C, area under the curve 6, day 1, given at 3-week interval), after which accelerated RT with a concomitant boost ("field-in-a-field") (1.8 Gy large fields and the boost dose 0.88 Gy) was administered in 23 fractions with 61.64 Gy and concurrent weekly P (45 mg/m$^2$). Consolidation with two cycles of PC was administered.

**Results:** The median follow-up for all 32 patients was 17.2 months (range, 3.8–107 months). The median survival time was 16.9 months, and the 5-year survival and 10-year survival were 25% and 17.5%, respectively. The median time for disease progression was 9.5 months, and disease-free survival was 21% at 5 and 10 years. The median time to local progression was 14.6 months, and the 5- to 10-year local progression-free survival was 35.7%. The median time to distant metastasis was 17.5 months. Toxicity was acceptable, with only one (3.1%) patient experiencing grade 5 (lung) toxicity and another patient presenting grade 4 toxicity (leucopenia).

**Conclusions:** The results of this single-institutional phase II study of induction CHT followed by concurrent RT-CHT and consolidation CHT in very unfavorable patient population showed acceptable results with acceptable toxicity.

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Radiochemotherapy (RT-CHT) is currently a recommended treatment approach for locally advanced inoperable stage IIIA and stage IIIB non-small cell lung cancer (NSCLC) in patients with good performance status (PS, 0–1).[1] A concurrent approach has been shown to be superior to sequential treatment delivery in the meta-analyses in terms of longer survival.[2]

In 2004, we published our experience[3] combining full-dose induction CH (cisplatin plus gemcitabine for two cycles) followed by concurrent administration of accelerated radiotherapy with a concomitant boost (with a total dose of 61.64 Gy administered in 23 fractions), with cisplatin and navelbine for two courses, finally followed by two courses of the same initial chemotherapy (CHT). The median survival was 15.4 months with an actuarial 1-, 2- and 3-year survival of 67, 21 and 15%, respectively. Hematological and esophageal toxicity ≥ grade 3 was not negligible (60% and 30%, respectively). The RT schedule consisted of an accelerated schedule using the concomitant boost technique.[4] This was achieved using a "field-in-a-field" technique (simultaneously integrated boost), whereby the larger area was treated to 1.8 Gy followed by a smaller area (boost) being treated with an additional 0.88 Gy with no time delay.

Preliminary reports of a phase I/II study by Uitterhoeve et al.,[5] which combined a daily low-dose CHT and a similar accelerated RT schedule, obtained an encouraging overall actuarial 1- and 2-year survival of 53% and 40%, respectively.

With this background, our aim was to make a new phase II trial to assess the safety, activity, survival, and progression-free survival after full-dose induction CH, concurrent RT-CHT based on accelerated RT with weekly paclitaxel (P), and full-dose consolidation CHT as induction therapy. Our hypothesis was that this phase II would reduce toxicity maintaining at least the same effectiveness as our