Lung cancer

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Randomized Pan-European trial comparing paclitaxel (TAX)/carboplatin (CAR) versus paclitaxel/cisplatin (CIS) in advanced non-small cell lung cancer (NSCLC)

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From April 96 to July 97, 618 patients (pts) with advanced NSCLC previously untreated with chemotherapy were randomized to receive TAX at a dose of 200 mg/m^2 (3-hr IV infusion) followed by either CAR at an AUC of 6 mg/mL.min or CIS at a dose of 80 mg/m^2. Courses (crs) were repeated every 3 weeks. Main objectives of this study were to assess whether response rate (RR) in the TAX/CAR arm was non-inferior to the TAX/CIS arm, and to compare safety between the two arms. Safety and survival analyses were done on all treated and all randomized pts respectively. Response analysis was done on response evaluable (measurable disease) pts. Pt characteristics were well-balanced between the 2 arms with regards to sex (83% male), age (median 58 yrs), performance status (66% ECOG 1, 18% ECOG 2), stage (69% IV, 31% IIIb) and histology (38% squamous). In the TAX/CAR arm, 306 pts received a total of 1311 crs (median 4, range 1–10) while in the TAX/CIS arm, 302 pts received a total of 1321 crs (median 4, range 1–10). In only 72% of crs, CAR was administered at an AUC of 6 (mostly due to miscalculation) while in 91% of crs, cisplatin was given at 80 mg/m^2. The response rate was 25% (70/279) in the TAX/CAR arm and 28% (80/284) in the TAX/CIS arm (90% CI for difference in RR: −10.0 to 3.4%). Responses were reviewed by an independent radiological committee. Median survival was 8.5 mths in the TAX/CAR arm and 9.8 mths in the TAX/CIS arm (HR = 1.20, 90% CI: 1.03–1.40) and one-year survival rates were 33% and 38% respectively. Excluding neutropenia, thrombocytopenia, nausea/vomiting and nephrotoxicity, the rate of severe toxicities was low and comparable between the 2 arms. Overall quality of life (EORTC QLQ-C30 and LC-13) was similar between the 2 arms. The study shows that TAX/CAR is not inferior to TAX/CIS in RR and can represent an alternative in the treatment of advanced NSCLC.

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Experience of an external radiological review committee during a randomized Pan-European trial comparing paclitaxel (TAX)/carboplatin (CAR) versus paclitaxel/cisplatin (CIS) in advanced non-small cell lung cancer (NSCLC)

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From April 96 to July 97, 618 patients (pts) with advanced NSCLC previously untreated with chemotherapy were randomized to receive TAX followed by either CAR or CIS. The main objective of this study was to assess whether response rate (RR) in the TAX/CAR arm was non-inferior to the TAX/CIS arm. An external radiological review committee was created to help determine the most accurate and objective response rate. Patients selected for the review had either a partial (PR) or a complete response (CR) as determined by the investigator. In addition, patients with borderline stable disease (SD) or ambiguous cases were also reviewed. Radiologists conducted the review without knowing the response claimed by the investigator nor knowing the treatment arm assigned to the patient. During 5 sessions, totaling 10 review days, the imaging films from a total of 265 patients (43%) were reviewed. In 194 patients (73%), the response was confirmed (e.g. PR...PR, CR...CR, SD...SD). In 55 patients (21%), the response was downgraded (e.g., CR...PR, PR...SD, SD...PD). In 16 patients (6%), the response was upgraded (e.g., SD...PR, PR...CR). The overall RR before review was 33% (8 CR + 194 PR/618 patients). After the review, the overall RR was 24% (6 CR + 144 PR/618 patients). Study related problems and tumor related problems were identified by the external committee as responsible for this difference in RR. In this study, the claimed overall RR was decreased by the external review committee by 9% (27% relative decrease). This underlines the importance of an external review in accurately determining the response in a study where response rate is the primary objective.

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The clinical relevance of the new UICC-staging (1997) for inoperable non-small cell lung carcinoma (NSCLC) treated with radiotherapy

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Purpose: The purpose of this study was to determine the prognostic value of the new UICC-staging (1997) in a subset of patients with inoperable NSCLC treated with radiotherapy alone and to compare it to the previous UICC-staging system.

Material & Methods: A total number of 1354 patients irradiated on intrathoracal tumour for inoperable NSCLC were included. According to the new staging system 67 patients (5%) had stage IA, 172 (13%) stage IB, 4 (1%) stage IIA, 146 (11%) stage IIB, 438 (32%) stage IIIA, 436 (32%) stage IIIB and 91 patients (7%) stage IV. Of the 146 patients with stage IIB, 128 patients had a T3N0M0 tumor and 18 patients had a T2N1M0 tumor.

Results: The median survival (MS) of all patients with stage I was 12.4 months. In stage IA the MS was 17.6 months which was significantly longer compared to 11.2 months in stage IB ($p = 0.0016$). The MS of the 18 patients with stage IIB (T2N1M0) was 8.0 months. In the new staging system, T3N0M0 is also classified as Stage IIB. The MS of these IIB patients was 8.6 months and did not statistically differ from the group of patients with stage IIIA in which a MS of 7.6 months was observed. The MS of patients with stage IIIB was 6.5 months and 4.0 months for stage IV cases.

Based on this multivariate analysis, three prognostic groups could be identified. The most favorable prognosis was observed in stage IA and IIA with a MS of 17.7 months. A difference of less than 10% was noted between stage IB, IIB, IIIA and IIIB. The MS in these groups together was 7.7 months. The most unfavorable group consisted of stage IV patients with a median survival of 4.0 months.

Conclusion: In patients with inoperable NSCLC treated with radiotherapy, the distinction between stages IA and IB in the new staging system is clinically relevant. The distinction between T3N0M0 and stage IIIA seems to be of less importance in patients treated with radiotherapy.

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Taxotere® (TXT) versus best supportive care (BSC) in chemonaive patients with unresectable non-small cell lung cancer (NSCLC): Final results of the phase iii study

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Objectives: To determine the effects of TxT on survival, clinical benefits, quality of life and safety parameters for chemonaive patients (pts) with advanced NSCLC, when compared to BSC (no chemotherapy or systemic anticancer therapy permitted).

From Oct. '95 to Dec. '97, 207 pts were randomized between the 2 arms, (2:1 allocations) with stratification by ECOG PS (0–1 vs 2) and stage (advanced vs metastatic). Eight countries (18 centers) did participate. 137 pts received TxT 100 mg/m" d1, 1 hour i.v. infusion, q 3-weeks, and 70 received BSC. Baseline characteristics are well balanced between the 2 arms. TXT superiority is clearly shown for survival, paricularly in later follow-up times: 6-month: 49% vs 46%; 12-month: 25% vs 16%; 20-month: 12% vs 0% (stratified log rank $p = 0.04$), for time to progression: median 12.6 vs 8.9 weeks ($p < 0.001$), and for Clinical benefit: improvement in pain and in dyspnea symptoms, less use of morphinics ($p < 0.001$), of non-morphine analgesic ($p < 0.001$), of other tumor related medication ($p < 0.01$) and of radiotherapy ($p = 0.01$). RR in the TxT arm is 20% [95% CI = 12; 29].

Conclusion: Single agent Taxotere® (100 mg/m" d1 q3-weeks) does improve survival and clinical benefit for patients with unresectable NSCLC.