# Diagnosis, Treatment and Prognostic Factors in Lung Cancer

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## IMPORTANCE OF CELLULAR PROLIFERATION MARKERS IN PREDICTING THE CLINICAL COURSE OF PATIENTS AFFECTED BY LUNG CARCINOMA

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Cellular proliferation rate has been investigated in 84 primitive carcinomas, 4 carcinoid tumors and 10 non neoplastic lesions of the lung. Ki-67 (Dako) and PCNA (Dako) by means of immunohistochemical methods, Ag NOR count and area by means of a silver staining technique and SPF by flow-cytometry were performed. Moreover, p53 (DBA) oncosuppressor gene-related protein expression and DNA-index were also detected. Ki-67, PCNA, AgNOR and p53 were automatically counted by an image analyzer. Lung carcinomas were set according to WHO (1981), Kreyberg (1976) and clinical (small cell and non small cell carcinoma) classifications. Patients were followed up over three years. Statistical analysis was performed using ANOVA, Student's T and chi-square tests. Clinical course does seem to closely correlate both with stage ($p< 0.0001$) and grade ($p< 0.005$) of the neoplasm. On the contrary proliferation markers do not seem to correlate to clinical course, even though advanced tumors exhibit higher AgNOR count ($p< 0.03$), as well as poorly differentiated tumors show higher PCNA ($p< 0.001$), Ki-67 ($p< 0.02$) and SPF ($p< 0.02$) values. Moreover, higher mean AgNOR area values ($p< 0.005$) were recorded in secerning tumors, while higher SPF values ($p< 0.005$) were counted in small cell carcinomas. In conclusion, our study underlines the prognostic significance of grading and staging in lung carcinoma and, moreover, it suggests a role for proliferation markers as prognostic indicators.

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## ASYMPTOMATIC PATIENTS WITH INOPERABLE LOCALIZED NON-SMALL CELL LUNG CANCER: RADIOTHERAPY NOW OR LATER?

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**Radiotherapy (RT) is a preferred treatment for patients with inoperable localized non-small cell lung cancer (IL-NSCLC), but is controversial for asymptomatic patients. To further define the role of RT in such patients, a retrospective comparison of the outcome of 41 persons who received RT immediately (group A) with that of 17 patients who were followed and treated after symptoms arose (group B) was undertaken. Although clinical features (i.e., disease stage, presence of significant weight loss, poor initial performance status, median age) differed ($p>0.10$) for groups A and B, the survival rate at 5 yrs was 12% and 0%, respectively, $p>0.10$. On the basis of these results, early RT appears to be beneficial in asymptomatic patients with IL-NSCLC.**

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## MICE: a new active combination for NSCLC

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From September 1989 to december 1993, 56 consecutive patients were enrolled to receivo: MITOMYCIN-C=6 mg/m², IFOSPHAMIDE=3 gr/m², CISPLATIN=75 mg/m² and VINDESINE=3 mg/m² i.v. on day 1, every three weeks. 50 patients are now evaluable for response and toxicity. Patients characteristics were as follow:

| Median age | Sex (M/F) | PS | Histology (Ade/ Squam/ Und ) | | |
|---|---|---|---|---|---|
| 55 | 52/4 | 0-3 | 21 | 33 | 2 |

Response to therapy, according to stage, were:

| Stage | N° pts | CR | PR | NC | PD | TTF / OS |
|---|---|---|---|---|---|---|
| III A | 10 | - | 8* | 2 | - | 22+ / 22,7+ |
| III B | 8 | - | 4 | 3 | 1 | 7,2+ / 10,6+ |
| IV | 32 | - | 17 | 9 | 6 | 5,3+ / 8,2+ |

*CR after surgery, with 2 pCR

Major toxicity WHO grade was: Anemia III=4pts, Leucopenia III=2 and IV=1, acute pulmonary edema (probably due to fluid overload)=2.

One pt. experienced paralytic ileus. Nausea and vomiting were generally mild or moderate.

MICE is a well tolerated combined treatment and is feasible on an outpatient basis.

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## THE VALUE OF BONE SCANNING IN THE STAGING OF NON-SMALL CELL LUNG CARCINOMA AND COMPARISON WITH THE OTHER PARAMETERS

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The curative treatment of non-small cell lung carcinoma (NSCLC) is surgery and the main point of staging is to select the operable patients. There are some conflicting data in the method of evaluation of bone metastasis (BM) in these patients in the literature. Some authors reported that bone scanning (BS) was not necessary in the patients in whom the clinical and biochemical findings of BM were negative while some others recommended BS in all patients. The aim of this study is to determine the value and necessity of BS in the staging of NSCLC.

Our study group comprised 80 patients with NSCLC. All patients were evaluated in terms of the symptoms and biochemical findings of BM and BS. The patients who had any positive sign of BM were underwent to further examinations such as X-rays and CT. Bone pain and/or tenderness were observed in 36 patients (45%) while 25 patients and 8 patients had elevated serum alkaline phospatase (AP) (31%) and calcium (14%) levels, respectively. BSs in 39 patients showed increased uptake (49%) and 28 of them were considered positive regarding BM (35%). BM in these patients was confirmed by X-ray and CT. Of these 28 patients, 18 had bone pain and/or tenderness (64%), 9 had elevated AP (32%), 4 had elevated calcium (19%).

Although the incidence of BM in the patients with bone pain was significantly higher than that in the patients without bone pain; 36% of the patients with BM did not show any sign of bone pain or tenderness. The positive and negative predictive values of bone pain in terms of BM were 50% and 77%, respectively. On the other hand, we observed BM in 25% of the patients who seemed in the early stages (Stage-I and II) before the evaluation for BM. Since thoracotomy was unnecessary in the advanced stages of NSCLC, the evaluation of BM should be done with the most sensitive procedures. For this reason, we recommend BS in the staging of all patients NSCLC according to our findings.