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COMBINED TREATMENT FOR ADVANCED EPIDERMOID CARCINOMA OF LUNG

Dómine M, Estévez L, Fernández Aramburo A, González Ageitos A, García Rico E, Lobo F, Vicente J. Universidad Autónoma de Madrid. Fundación Jiménez Díaz. Departamento de Oncología. SPAIN.

Twenty eight previously untreated patients (pts) with epidermoid carcinoma of lung stage III_A and III_B were prospectively treated with Cisplatin 120 mg/m^2 IV day 1, 5-Fluoruracil 1000 mg/m^2 continuous infusion days 2 to 6, Bleomycin 5 units IM days 1 to 5. Courses were repeated every 21 days. All pts received 3 cycles of this combination and were evaluable for response and toxicity. After chemotherapy 1 pts was treated with surgery and 27 with thoracic radiotherapy.

Twenty seven pts were male and 1 female. Median age was 64 years (range 34 - 73). All pts had an ECOG performance status 0 or 1. 10 pts had stage III_A and 18 III_B.

Twenty pts (71%) responded to chemotherapy. Complete remission (CR) was obtained in 7 pts (25%) and partial remission (PR) in 13 pts (46%). Two pts who achieved PR with chemotherapy obtained a CR with subsequent treatment (1 with surgery and 1 with radiotherapy). Median survival for all pts was 12 months, 14 months for stage III_A and 12 months for stage III_B (p= NS). Projected survival at 21 months was 17%. Three pts are alive and free of disease at 24, 49 and 58 months.

Toxicity was moderate . Mucositis (Grade II-III) was present in 14% of pts. One pts (3.5%) had renal toxicity (Grade I). Neutropenia (Grade II-III) was present in 6% of cycles and anemia in 11%.

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MVP CHEMOTHERAPY + RADIOTHERAPY VERSUS RADIOTHERAPY ALONE ± THYMOPENTIN IN ADVANCED NON SMALL CELL LUNG CANCER: A RANDOMIZED ITALIAN STUDY.

d'Aquino S., Adamo V., Altavilla G., Formosa A., Giusto M., Marchetti G., Pacilio G., Perego R., Russi. E.G., Schiraldi G., Tucci E.
Coordinator Center: Ist. Clin. Oncologica - Università di Messina

Thoracic radiotherapy (RT) is the standard treatment for inoperable stage III NSCLC giving unsatisfactory median survival of 9.5 months, with a five year survival of less than 5%. The association of Mitomycin C (MMC), Vindesine (VDS) and CDDP, (MVP), used as neoadjuvant therapy, showed a response rate of 68.8%. Thymopentin(TP5), a synthetic thymic hormone, has been able to inhibit cancer growth and reduce metastatic diffusion in murine models. The aim of our randomized and controlled study was to evaluate the effect of MVP + radiotherapy (CT + RT) versus RT alone, (Phase I), in terms of clinical response , survival and quality of life, and the TP5 effects in responders to RT ± CT (Phase II) in terms of time to progression, survival and quality of life. Since May 1990, 12 italian oncologic centers registered 146 pts with previously untreated stage IIIa (N2) or IIIb NSCLC. Pts have been randomly allocated, for phase I study to receive RT alone at total dose of 60 Gy/6 weeks, or CT (MMC 8 mg/m2 i.v. d 1-29, VDS 3 mg/m2 i.v. d 1-29) followed after 21 days, by RT as above. Responders were randomized, for phase II study to receive TP5 (50 mg s.c. every other day x 1 year) or nothing. Up to date, 95 pts are evaluable for phase I, 51 pts (group A) received RT alone, and 44 (group B) received CT + RT. Pts were well balanced for age, sex, stage (IIIA/IIIb) and PS. 35% of group A had OR (CR 2, PR 16), 48% of group B had OR (CR 4, PR 17). Survival rate was equivalent in both groups. Tolerance was substantially similar and acceptable in all patients.

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ORAL ETOPOSIDE IN THE MANAGEMENT OF MALIGNANT PLEURAL MESOTHELIOMAS PHASE II STUDY

E Kaukel (1), G Koschel (1), U Gatzemeier (2), J v Pawel (3), L Beckmann (4)
Dept. of Pneumology, Municp. Hospital Hamburg-Harburg (1), Dept. of Pneumology, Hospital Großhansdorf (2), Dept. of Pneumology, Hospital Gauting München (3), Bristol-Myers-Squibb GmbH, München (4) FRG

Malignant Pleural Mesothelioma is a highly treatment resistant tumor. Because there is a substantial need for new active cytotoxic drugs for the management of this disease we carried out a phase II study to evaluate the activity of oral Etoposide. Between 10/91 and 6/92 33 previously untreated pts with histologically proven malignant mesothelioma were treated with Etoposide 100 mg oral dy 1-14, every 3 weeks. Pts characteristics: male/female 32/1, median age: 61 (range 42-77), asbestos exposure 85%. Treatment toxicity was mild. 129 cycles have been administered (3.9 per pts), (WHO: nausea /vomiting 2°/3° 12%/3%, alopecia 2°/3° 30%/6%, leucopenia 2° 10%. Results: 31 pts. evaluable, 9,7% PR an 9,7% MR were achieved. The median duration of remission was 7 months. At present 11 pts are still alive (9,9,10,10,11,12,12,13,13,13,17 months). We conclud that Etoposid orally administered in this dosage is marginally effective in pts. with malignant PLM. The toxicity is mild. It is too early to assess duration of survival.

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MITOMYCIN/VINDESINE IN THE TREATMENT OF ADVANCED NON-SMALL-CELL LUNG CANCER -PHASE IV STUDY-

G Koschel (1), E Kaukel (1), B Waberzeck, S Halir, I Dittrich, U Dietrich
Dept. of Pneumology, Municp. Hospital Hamburg-Harburg (1) FRG

From 7/90 to 10/92 pts with stage IV NSCLC were treated with Mitomycin C 10 mg/qm day 1 i.v. and VDS 3 mg/qm day 1+8 i.v., every 4 weeks. All pts received at least one cycle an were eligible for toxicity. 262 pts were evaluable for response and 234 for survival. Pts characteristics: male/female 83% / 17%, median age 59,2 (range 33-81), med. KI: 70 (range 50-100). Histology: 108 adenocarcinomas, 98 squamous, 41 large cells, 8 mixed, 17 unclassified. A total of 784 cycles (median 3 per pts) has been administered with no evidence of severe side effects. Toxicity was as follows (WHO grade): Leucopenia 3°/4° 3%/1%, anaemia 3°/4° 7%/1%, nausea/vomiting 2°/3° 6% 0. 3% alopecia 3°/4° 6% 0.3%, neurotox 2°/3° 4% 0.4%, pulmonary tox. 2°/3° 3% 1%. Objective response (CR and PR) has been observed in 24%. The median survival for all patients was 6 months, for responding pts 9 months. These results indicate, that Mitomycin C/Vindesine is an active regimen with low toxicity in the treatment of advanced NSCLC. It is a reasonable alternative to more toxic, but not more effective Cisplatin containing regimen.

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PROGESTERONE RECEPTORS IN NSCLC. DO THEY HAVE A PROGNOSTIC SIGNIFICANCE?

K.Zarogoulidis, E.Ziogas, A.Papazoglou, H.Vainas, K.Dimitriadis, E.Paulidou, O.Antonoglou, Ch.Papaconstantinou, K.Manziou, K.Markopoulou.
Macedonian Lung Cancer Research Cooperative Group,Thessaloniki, Greece.

The role of human lung as an endocrine organ is well established. Lung cancer tissue probably has similar properties as shown by the presense of various hormone receptors in lung cancer cells. During the last 5 years we measured 4 steroid hormone receptors in malignant lung tissue taken from 54 patients who underwent surgical treatment for NSCLC. The steroid receptors measured in Fmls/mg of protein were those for estrogens (ER), progesterone (PgR), androgens (AR) and cortisol (COR-R) and overall percent positivity was 21%, 42%, 76%, and 21% respectivelly. 15 of these patients are already followed up for a period longer than 3 years. 7 of them had PgR values higher than 30 Fmls (30-1050) and are all alive, while the other 8 patients had values ranging from 0 to 20 Fmls, of whom 7 are already dead, the difference in death rate beeing highly significant ($p<0.001$). No such relationship was noted with the other 3 type of receptors. It seems that detection of high PgR values in NSCLC patients is a favorable prognostic factor but that needs to be confirmed by following up the rest of the patients. Perhaps the admininistration of hormonal treatment will further improve the outcome of PgR positive patients.

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Results of a phase II study using MIP regimen (Mitomycin+Ifosfamide+Cisplatin) in unresectable Non Small Cell Lung Cancer.JP. Dutin, H.Lacroix, N.Donnadieu, I.Cumin and G.Dabouis. Service d'Oncologie Médicale, Hôpital Laënnec, CHU Nantes 44035, France.

Between May 1991 to November 1992, 91 patients (pts) were enrolled in this study in a single institution in order to evaluate toxicity and efficacy of MIP regimen (Mitomycin C=6 mg/m2+Ifosfamide=3g/m2+Cisplatin=80mg/m2, Day 1, every 3 weeks). Patients caracteristics were the following:mean age=57 years(32-76), Performance status(OMS):0=22/91pts(24%), 1=45/91(49.5%), 2=24/91(26.5%), Stage:I=3/91(3.5%), IIIA=16/91(17.5%), IIIB=16/91, IV=56/91(61.5%), Histology: squamous cell carcinoma=56/91(61.5%), adenocarcinoma=43/91(47.5%), Large cell=11/91(12%). Patients were evaluated for response after 3 courses. Stage IV responders were continued until 6 courses depending on PS. Non metastatics patients underwend radiotherapy after 3 courses. Mean duration of chemotherapy treatment was 7 weeks. In 89 evaluable pts results are the following: complete response=4/89(4.5%), partial response=24/89(27%) so objective response is 28/89(31.5%), stable disease=44/89(49.5%), progression=17/89(19%).Main toxicity was hematological(Grade III-IV): 36/91pts(39.5%) neutropenia(2 toxic deaths), 11/91(12%) thrombopenia. No renal and neurological toxicity >2. 1 toxic death by pulmonary fibrosis(6 courses of Mitomycin). Median survival is not yet reached(February 1993). In conclusion, in spite of poor prognosis of this population(including brain metastasis) this regimen administrated on 24 hours every 3 weeks is effective and few toxic.