Conclusion: This novel treatment is well tolerated and highly active in limited SCLC.

1006 POSTER

The role of TC-99m tetrofosmin (T) SPECT in primary lung cancer (LC) detection

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Purpose: The aim of the study was to further evaluate the usefulness of Tetrofosmin-SPECT in identifying primary lung cancer.

Methods: After T injection, SPECT images of the chest were acquired in 122 pts with suspect pulmonary lesions at conventional imaging procedures. Scan data were analized qualitatively and semiquantitatively, the latter by calculating the Tumor/Background ratio (T/B) in the coronal slices, and were then related to histology.

Results: T-SPECT was true positive in 105/105 LC pts (sens. 100%) and true negative in 13/17 pts with benign pulmonary lesions (spec. 76.5%). T/B value was higher in malignant lung lesions than in benign ones (2.37 ± 0.84 vs 1.42 ± 0.24; $p < 0.05$). Considering a T/B cut-off value of 1.4, T-SPECT specificity increased to 88.2%.

Conclusion: T-SPECT appears a highly sensitive method in primary lung cancer detection since there was no false negative result in our cases. Moreover, the additional use of T/B seems to give more useful information in differentiating malignant from benign pulmonary lesions.

1007 POSTER

Chemoradiotherapy for advanced non-small cell lung carcinoma (NSCLC). Qualitative and quantitative evaluation of the literature

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Purpose: The treatment of unresectable stage III NSCLC by chest irradiation with or without chemotherapy remains controversial. In order to clarify the role of each therapeutic modality, we performed a systematic review of randomised trials on this field.

Methods: We assessed the selected studies for their quantitative therapeutic results. A qualitative overview was carried out using two scales: the Chalmers and the ELCWP (Lung Cancer 19:141;1998) scores. The ELCWP score includes 15 groups of items, 7 on internal validity and 8 on external validity (maximal theoretical score of 110 points).

Results: Ten studies were eligible for our analysis, including 1749 eligible patients. Five were significantly in favour of combined treatment. Overall median ELCWP and Chalmers scores were respectively 63.2% (range: 36% to 85%) and 49.2% (range: 29.3% to 71.6%). However, no statistically significant difference in methodology was found between negative ($p > 0.05$ on survival curves) and positive trials ($p \leq 0.05$ on survival curves) as well for the ELCWP or the Chalmers scores. No difference could be detected according to the number of eligible patients, the date of first registration or publication.

Conclusions: These methodological similarities allows to aggregate the results of the tested treatments.

1008 POSTER

Extensive clinical experience with Taxotere® (T) in 1st and 2nd line treatment at 100 mg/m² in locally advanced or metastatic NSCLC

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100 centers from Europe, Middle East, Asia and South America participated in NSCLC study with broad inclusion criteria (1st + 2nd line) to establish the toxicity and efficacy profile of docetaxel at 100 mg/m² in worldwide clinical practice. 754 patients (pts) have been treated, 585M/169F. 3023 cycles have been administered, median: 3 (1–12). Median age was 59 yrs (25–83), median WHO PS: 1 (0–3), Median number of organs involved: 2 (1–6). Adenocarcinoma: 313 pts, squamous cell: 235 pts, large cell: 35 pts, other: 171 pts.

Results: To date 536 patients are evaluable for reponse, the overall response rate in first line is 27.9% (95% CI [17.5–29.8]). Safety profile: neutropenia gr. 3/4: 55% of pts, non hematologic toxicities gr 3/4: infection 5%, diarrhea 4%, pulmonary 3%, skin 2%, stomatitis 2%, neurosensory 3%

Conclusion: The safety and efficacy reported in more limited studies is maintained in a broad population.

1009 POSTER

Bendamustin in untreated small cell lung cancer (SCLC): Efficacy and toxicity

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Purpose: High response rates can be induced in patients (pts) with SCLC by different cytostatic treatment regimens. Durable remissions, however, are rare, even after aggressive and toxic combinations. Therefore, at least equally effective but less toxic first line treatments are warranted.

Methods: Twenty-six pts with extensive disease (ED) SCLC and no prior treatment received Bendamustin 120 mg/m² as an one-hour infusion on two consecutive days. The treatment was repeated every three weeks. If a complete (CR) or partial (PR) remission was achieved, six treatment cycles were given. In case of "no change" (ND) therapy was terminated after 4 cycles. It was immediately stopped, if disease progression (PD) could be demonstrated at regular tumor evaluations prior to every new treatment cycle.

Results: So far, 22 pts are evaluable for response and toxicity. Two pts (9%) showed CR, 8 pts (36%) PR and 4 pts (19%) NC. Another 8 pts (36%) had PD. The median remission duration is 3+ months (range, 1+–5). The median survival time is not achieved. Side effects (preferably WHO grade 1 and seldom 2) restricted to myelosuppression and gastrointestinal toxicities.

Conclusion: Bendamustin is a very effective and well-tolerated agent in ED SCLC. Remission durations are comparable to more aggressive and toxic cytostatic combinations.

1010 POSTER

Unresectable non-small cell lung cancer (NSCLC) as a target for clinical trials of AG3340, a selective inhibitor of matrix metalloproteases (MMPs), in combination with standard chemotherapies

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While treatment of newly diagnosed, advanced stage NSCLC with combination chemotherapy commonly results in patient benefit, therapies that enhance outcome are needed. MMPs are a family of enzymes that degrade the matrix between cells. Several of these enzymes have been shown to facilitate tumor angiogenesis, invasion, and metastasis. AG3340 is a potent and selective inhibitor of MMPs designed using X-ray crystallography. AG3340 inhibits MMP-2, -9 and -14 with Ki values of 30–330 pM, but is less potent against the enzyme believed to be responsible for maintaining function in the joints (MMP-1, Ki 8300 pM). Preclinical experiments conducted in xenograft tumor models demonstrated antitumor effects of single agent AG3340 and enhanced efficacy of chemotherapy and radiation therapy when administered in combination with AG3340. The pharmacokinetics of AG3340 in volunteers and patients are similar and linear, the free fraction in plasma is high (31%), and the minimum effective concentration identified in preclinical models is easily exceeded with well-tolerated doses of AG3340 administered twice daily. Two randomized, double-blind, placebo-controlled Phase III studies in patients having newly diagnosed Stage IIIB/IV or recurrent NSCLC are underway in North America, Europe and Australia. AG3340 or placebo is administered beginning on Day 1 of the study in combination with standard doses and regimens of gemcitabine/cisplatin or paclitaxel/carboplatin. Because AG3340 might be expected to slow the rate of tumor growth beyond an arbitrary definition of progression, patients may continue treatment with study tablets (AG3340 or placebo) in combination with the investigator's choice of subsequent therapies, in hopes of providing additional survival benefit. As of March, 1999, 400 patients have been accrued at over 50 participating institutions. Therapies used subsequent to first-line therapy and in combination with study tablets have

included vinorelbine, cisplatin, etoposide, docetaxel, mitomycin, vinblastine and radiation therapy. All combination regimens have been well tolerated with no evidence of AG3340-related enhancement of toxicity. Accrual to these Phase III studies and studies in other diseases continues.

1011 PUBLICATION

Preliminary results of a dose-intense phase II study of a combination chemotherapy regimen with cisplatin (CDDP) and epirubicin (EPI) including medroxyprogesterone acetate (MPA) and recombinant interleukin 2 (rIL-2) in patients with inoperable primary lung cancer

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Based on our previous experimental and clinical data (G. Mantovani et al. Semin Oncol 25 (suppl 6): 45–52, 1998), we carried-out an open, dose-finding phase I study of a com-bination chemotherapy regimen (weekly CDDP + EPI) including rIL-2 and MPA for 6 weeks in 16 patients (pts) with stage IIIB–IV inoperable primary lung cancer. The maximum tolerable dose (MTD) was: CDDP 40 mg/m^2/week (w) and EPI 40 mg/m^2/w. A phase II study in the same patient population was designed with clinical response and toxicity as primary endpoints. The treatment schedule was: CDDP 40 mg/m^2/w on day 1, EPI 40 mg/m^2/w on day 1, MPA 1 g/day orally on days 1 to 7 starting 1 week before the 1st cycle and rIL-2 1.8 MIU administered subcutaneously (SQ) on days 2 to 6, for 6 weeks. G-CSF support 300 μg SQ was administered on days 2 to 5. From March to December 1998, 29 pts were enrolled: all were evaluable for toxicity and 22 of them for response as at February 1999 (M/F: 19/3, mean age: 68, range: 37–76). All patients but 3 had Stage IIIB–IV primary lung cancer (21 pts NSCLC and 1 pt SCLC). 90% pts had ECOG-PS. The body weight, appetite and QL (Therapy-Impact Questionnaire) were also evaluated. After 6 weeks, 10/22 patients (45.5%) had PR, 10/22 (45.5%) SD and 2/22 (9%) PD: the ORR was 45.5%. ECOG PS and body weight did not change significantly after treatment, whereas appetite showed a slight increase. Toxicity was only hematological. Grade 3/4 toxicity recorded were: 4 Grade 3 anemia and 2 Grade 3 leukopenia. One acute miocardial infarction occurred. Among the cytokine studied (IL-1β, IL-2, IL-6, TNF α), only IL-1 β serum levels were decreased after treatment. The study is in progress. *Work supported by C.N.R., Rome, A.P. "A.C.R.O." Contract no. 96.00588.PF39.*

1012 PUBLICATION

A phase II study of gemcitabine plus oral etoposide (GOE) in treatment of advanced non-small cell lung cancer

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Purpose: We have designed a new non-cisplatin based chemotherapy regimen to capitalize on the mild toxicity of gemcitabine (a novel antimetabolite) in treatment of advanced non-small cell lung cancer (NSCLC). This combination chemotherapy is intended to be relatively non-toxic and simple in administration. In this phase II study we report the response rate, toxicity, time to disease progression and survival.

Methods: Inclusion criteria: age 18 to 75; histologically confirmed NSCLC; stage IIIb or IV disease; bi-dimensionally measurable; chemotherapy naïve; no radiotherapy within 3 weeks of enrollment; ECOG performance status of 0 to 2; and informed consent. Patients with CNS metastasis, hypercalcemia, abnormal renal function and life threatening medical condition were excluded. Eligible patients were treated with gemcitabine 1000 mg/m^2 IV at day 1, 8, and 15 plus oral etoposide 50 mg daily from day 1 to 14 (GOE14) which was increased to 21 days (GOE21) if there was no WHO grade 3 toxicities in the first 2 cycles (28 days cycle).

Results: Between 5/97 and 7/98 we enrolled 46 patients and 44 were evaluable. Patient characteristics: mean age 53.4; male 37; female 7; stage IIIb 27; stage IV 17. One hundred and eleven courses of GOE14 and 100 courses of GOE21 were delivered. The incidence of grade 3 WHO toxicity is as follow: anemia 29.6%, leukopenia 29.5%, neutropenia 31.7%, thrombocytopenia 18.2%, nausea and vomiting 6.8%, mucositis 0%, and proteinuria 4.5%. Only 2 patients had neutpenic sepsis and both recovered promptly with antibiotic. No septic death was reported. Responses were 1 complete (CR 2.3%) and 19 partial (PR 43.2%). There were 12 stable disease (SD 27.3%) and 12 progressive disease (PD 27.3%). Median time to progression and median survival was 26 and 49.7 weeks respectively. One-year survival rate was 45%.

Conclusion: This new combination chemotherapy of gemcitabine and oral etoposide achieves high response rate. Comparing to historic data of other cisplatin-based regimens the toxicity of this combination is less and the survival is similar if not better.

1013 PUBLICATION

Accelerated hyperfractionation radiotherapy concurrently combined with chemotherapy for stageIII non-small cell lung cancer

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Purpose: StageIII non-small cell lung cancers (NSCLC) were treated with concurrent accelerated hyperfractionation radiotherapy (AHFRT) and chemotherapy to evaluate its feasibility and efficacy.

Methods: Fifty-seven patients with stageIII NSCLC who treated from 1992 to 1997 were enrolled in this study. They consisted of 53 males and 4 females, and ranged in age from 36 to 79 years (mean 65 years). Seven of them were stageIIIA and the others were stageIIIB. With the maximum dose of 60–72 Gy as a goal, AHFRT was performed twice per day at a dose of 1.5 Gy or 1.8 Gy for each irradiation. This was combined with chemotherapy using Cisplatin (80–160 mg/m^2) or Carboplatin (300–600 mg/m^2) as a principal anticancer agent.

Results: The treatment could be completed in 54/57 (95%). The major acute toxicity encountered was grade 3 or greater leukopenia (32/57; 56%) and esophagitis (7/57; 12%). In patients of 1.8 Gy group, esophagitis appeared frequently (6/27; 22%) as compared with patients of 1.5 Gy group (1/30; 3%). Grade 2–3 radiation pneumonia was encountered in 18/52 evaluatable patients (35%). No grade 4 or greater radiation pneumonia was encountered. The primary effects in patients in whom the treatment was completed were rated as complete response in 2 (4%), as partial response in 44 (81%) and as no change in 8 (15%). Response rate was 85% in over all. The 1, 3 and 5-year rates were 63%, 25% and 16% respectively.

Conclusion: AHFRT (1.5 or 1.8 Gy at each irradiation for 60–72 Gy) concurrently combined with chemotherapy using Cisplatin (80–160 mg/m^2) or Carboplatin (300–600 mg/m^2) was appeared feasible with a tolerable degree of toxicity and is expected to contribute to the improvement of StageIII NSCLC.

1014 PUBLICATION

Vinorelbine, carboplatin and gemcitabine (VGC) in the treatment of untreated advanced/metastatic non-small cell lung cancer (NSCLC): A phase I study

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Background: Vinorelbine (VNR), Carboplatin (C) and Gemcitabine (GEM) are drugs which are active in the treatment of NSCLC. Administration of these three drugs can be a valid alternative to compounds containing cisplatin.

Purpose: To determine the maximum tolerate dosed (MTD) of C in association with fixed doses of VNR and GEM.

Methods: The study enrolled patients with Stage III B and IV, non-pretreated, inoperable NSCLC that could not be treated with radical radiation therapy; age < 70, PS < 2 (ECOG), with normal hepatic, renal and hematological function, the patients gave informed consent. The patients were treated with increasing doses of C at day 1. Treatment cycles were repeated every 4 weeks. The dosage of C was calculated on the size of the AUC using Calvert's formula. The starting dose corresponded to AUC 4; doses of C corresponding to AUC 4-4,5-5-5,5 and 6 were tested without unacceptable toxicity.

Results: 24 male patients were enrolled, at 5 different dosage levels for a total of 78 cycles. The mean age was 60 years (47–70). Mean PS 1 WHO (0–2). Grade 3 neutropenia was found in 2 patients at AUC 5 and in 2 patients at AUC 5,5 of C. The MTD was found at AUC 6 with grade III–IV thrombocytopenia in 3 of the 6 patients treated.

Conclusions: The recommended dose of C for a Phase II study is AUC 5,5.