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.