DLTs were defined as follows: an absolute neutrophil count (ANC) < 500/ul for >7 days or <100/ul for 3 days; febrile neutropenia; any grade ≥ 3 (WHO) non-hematologic toxicity. Ventricular ejection fraction (LVEF) was evaluated by bidimensional ecocardiography (or MUGA scan) at entry and at the end of treatment. Twelve untreated pts with extensive-disease (ED) SCLC entered the study and were evaluable for toxicity. Median age 65 (range 61–70), median ECOG PS = 0 (range 0–1); six pts (50%) had brain metastases and 3 (25%) presented bone marrow involvement. Hematologic toxicities (WHO) are summarized below:

EpiDx	P	n. Pts	n. courses	ANC G4 (%)
60	155	3	18	/
75	155	3	18	/
90	155	3	18	11
90	175	3	11	27

No episode of febrile neutropenia was observed; only one pt with bone marrow involvement experienced grade 3 anemia and thrombocytopenia after the fifth course of CT. Baseline median EF was 63.3% (range 57–70%) and no significant modification was observed at the end of treatment. Even if activity was not the main end-point of the present study, responses were assessed every 3 courses: six out of 12 pts showed a complete response (CR) and 6 pts a partial response (>75%). Pts with celebral metastases received whole brain irradiation (30–36 Gy) concomitantly with chemotherapy courses and obtained a CR. In conclusion, the combination of P, EpiDx, E at optimal doses is feasible and its toxicity profile compares favourably with other three-drug-regimens commonly used. The mild and easy-to-manage hematologic toxicity reported make it possible for this regimen to be safely integrated with radiotherapy. In addition, this triplet shows promising antitumor activity. A multicenter phase II study is in progress in order to better define the antitumor activity of the combination.

1024 PUBLICATION

Paclitaxel, gemcitabin, and cisplatin in non-resectable non-small cell lung cancer (NSCLC)

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Purpose: To evaluate the activity of a new 3-drug chemotherapy regimen in a phase II study in patients (pts) with NSCLC.

Methods: Inclusion criteria were: Non-resectable NSCLC, no prior chemotherapy, no brain metastases, performance status 2 or better, normal organ function, and measurable disease. Doses and schedule were: Gemcitabin 1000 mg/m^2 i.v. day and 8, Paclitaxel 180 mg/m^2 i.v. day 1, and Cisplatin 100 mg/m^2 i.v. day 1, every weeks.

Results: Pretreatment characteristics for 29 included pts were: Female/male ratio 15/14; median age 58 years (range 42–68); stage IIIA 14%, IIIB 48%, IV 38%; performance status 0 44%, 1 28%, 2 28%; adenocarcinoma 62%, squamous cell 24%, large cell 3%, adenosquamous 7%, unclassified NSCLC 3%. 27 pts were evaluable for toxicity, which was mainly hematological with WHO grade III or IV neutropenia in 92% of pts, and thrombocytopenia in 63%. Non-hematologic grade WHO grade III toxicity were: nausea/vomiting 41%, neurotoxicity 7%, nephrotoxicity 26%, while none had grade IV non-hematological toxicity. There were 12 episodes of febril neutropenia in 11 pts with 1 toxic death, and 4 bleeding episodes in 4 pts. Among 22 pts evaluable for response there were 12 partial, and 1 complete response (59%, 95% confidence limits 36–79%). Median time to response was 12 weeks and median response duration 21 weeks (range 10+–50+ weeks).

Conclusions: This new 3-drug regimen in NSCLC seems promising, with a substantial number of long lasting responses. Toxicity was generally manageable, though pronounced, and modifications might improve the feasibility. The study is ongoing to 40 evaluable patients.

1025 PUBLICATION

Gemcitabine monotherapy in elderly advanced NSCLC patients

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In phase II trials Gemcitabine (Gem) showed to be an active agent in NSCLC, producing a clinical benefit often higher than response rate.

We assessed the impact of Gem treatment in obtaining therapeutic response and better quality of life in 21 untreated ederly patients (aged >70 years) with NSCLC, enrolled from 1/87 to 8/98. The main characteristics of patients were: M/F 18/3; median age 74 years; stage III B 7, IV 14. The schedule was: Gem 1250 mg/sm i.v. days 1–8 q. 21 days. Response and toxicity have been analyzed according WHO criteria. Clinical benefit has been evaluated by patient visual analogue symptoms score, the ECOG Performance Status and weight.

All patients are evaluable: we found 7 PR (33%), 5 SD (24%) and 9 PD. WHO grade 2 leukopenia (in 4 pts) and trombocytopenia (grade 3 in 1 pt. and grade 2 in two pts.) have been the main toxic effects. A clinical benefit has been demonstrated in all 12 patients with PR or SD and in 3 patients with PD.

These data confirm that Gemcitabine monotherapy is a well tollerated and active therapeutic approach in ederly NSCLC patients and stress its role in determining a clinical benefit.

1026 PUBLICATION

Combination of docetaxel and gemcitabine in the treatment of advanced non-small cell lung cancer (NSCLC)

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Docetaxel and gemcitabine are two of the most active single agents in the treatment of non-small cell lung cancer (NSCLC). The purpose of the study was to evaluate the tolerance and efficacy of the combination containing these two drugs in the treatment of patients with advanced NSCLC.

Twenty-three patients with NSCLC stage IIIb or IV, median age 60 years (range 36–69) entered the study till now. The male/female ratio was 16/7. Six of the patients were treated previously with first-line chemotherapy including cisplatin or carboplatin. In the present protocol chemotherapy was administered in a three-week treatment cycle in which docetaxel was given on day 1 and gemcitabine on days 1 and 8 with a maximum of 6 cycles per patient. The patients were treated at three dose levels: 1): docetaxel 75 mg/m^2 and gemcitabine 800 mg/m^2 (including only the pre-treated patients), 2): docetaxel 80 mg/m^2 and gemcitabine 800 mg/m^2 and 3): docetaxel 80 mg/m^2 and gemcitabine 900 mg/m^2. Six patients entered at dose level 1, twelve at dose level 2 and five at dose level 3. Neutropenia NCI-grade 3 or 4 was observed at all dose levels (at dose level 3 in two of five patients). Diarrhoea NCI-grade 3 was seen in four patients (three at dose level 1 and one at dose level 3). Diarrhoea grade 2 was seen in five patients at dose level 2.

Maximal tolerated dose has been reached at dose level 3 with three of five patients experiencing grade 3 or 4 side effects (neutropenia (2) and diarrhoea (1)). Of twenty-two patients evaluable for response partial response was achieved in nine (39%). The recommended dose for phase II-trials is docetaxel 80 mg/m^2 (day 1) and gemcitabine 800 mg/m^2 (day 1 and 8) in a three-week cycle. The study is ongoing including patients at dose level 2 and evaluating the patients' self-reported quality of life.

1027 PUBLICATION

A phase II study of paclitaxel (P) and carboplatin (C) as second-line treatment in patients (PTS) with small-cell lung cancer (SCLC)

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Background: There is no standard treatment for pts with SCLC relapsing after first-line therapy. Both P and C have demonstrated activity in this setting and there is evidence of synergism between these agents. We conducted a phase II study to evaluate the efficacy and toxicity of P and C combination as second-line treatment in patients with SCLC. Patients and treatment: Twenty-one SCLC pts (18 male, 3 female) progressing after first line chemotherapy were enrolled. Front-line treatment included cis-platin and etoposide (17 pts) and cyclophosphamide, adriamycin and vincristine (4 pts). All but 3 pts (85%) had disease progression or relapse within 3 months after front line therapy (refractory disease). P (200 mg/m^2) was administered on day 1 as 3 hr iv infusion, and C at 6 AUC (Calvert formula) iv on day 2, cycles repeated every 4 weeks. rhGCSF was administered prophylactically in case of previous grade 3/4 neutropenia. The median age was 63 years (range 43–77); PS (WHO) was 0 (6 pts), 1 (13 pts) and 2 (3 pts).

Results: Eighteen pts were evaluable for response and 21 for toxicity. Grade 3/4 neutropenia without fever was observed in 6 (28%) pts. Thirteen pts (61%) required GCSF. Two pts (10%) developed non-neutropenic fever.