CNS metastases were excluded. VNR administered on d1, 8, 15; CBDCA on d1 according Chatelut AUC. Cycles repeated every 28 d. 3 planned dose levels: 1st) VNR 25 mg/m^2 + CBDCA 6, 2nd) VNR 30 mg/m^2 + CBDCA 6, 3rd) VNR 30 mg/m^2 + CBDCA 7. 3–6 p treated at each level according observed toxicity. MTD: G3–4 toxicity CALGB criteria in 2/3 of p (excluding vomiting and alopecia). Weekly CBC. Response assessment after 2nd cycle.

Results: 14 p have been treated. Sex ratio M/F: 13/1. Median age: 58 y (43–69). PS 0/1: 2/12. 39 cycles have been delivered. Non-hematologic toxicity was mild: G3 mucositis in 2/14 p (14%), G2 peripheral neurotoxicity in 3/14 p (21%). Predominant toxicity was myelotoxicity with neutropenia G3 22/39 cycles (56%) and G4 (6/39 cycles (15%), but neutropenic fever occurred only in 4/14 p (28%) or 5/39 cycles (12%). Anemia G3–4 appeared in 1/14 p (7%). Thrombopenia G3 in 4/14 p (28%) and 10/39 cycles (26%). Only 1 p developed G4 thrombopenia. Median neutrophil count was 2100/mm3 d8, 980 d15 and 1310 d21. VNR needs to be reduced in 38/117 (32%) planned doses and omitted in 10 (8%). Delivered VNR DI has been 11 mg/m^2/w (planned 18.75 mg/m^2/w). At 1st level 3/6 evaluable p developed G3–4 toxicity. In 2nd level 4/6 evaluable p suffered G3–4 myelotoxicity. Overall response (PR) in 8/12 evaluable p (66%).

Conclusion: With this schedule CBDCA-VNR combination MTD was reached at 2nd level (VNR 30 mg/m^2 d1, 8, 15 + CBDCA AUC 6 d1 every 28 d). This combination is active but in this subset of p, toxicity seems too high to continue development of this schedule in Phase II trial.

1037 PUBLICATION

A phase II study of irinotecan and infusional cisplatin with recombinant human granulocyte colony-stimulating factor (rG-CSF) support for advanced non-small cell lung cancer (NSCLC)

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Purpose: We administered chemotherapy consisting of a combination of 5-day continuous infusion of cisplatin (20 mg/m^2/day) plus irinotecan (160 mg/m^2/day, as a bolus, on day 1) with rG-CSF support in previously untreated advanced NSCLC patients, and evaluated the effectiveness and safety of this therapy.

Material: Forty-one NSCLC patients were enrolled.

Results: Twenty-four patients achieved a partial response. The response rate was 58.5% (95% confidence interval, 42.2% to 74.8%), with a median response duration of 32.1 weeks. The median survival time was 44.8 weeks and the 1-year survival rate was 44%. A total of 100 courses of therapy were given. The major toxic effects were grade 3 or 4 diarrhea (23%), granulocytopenia (20%), thrombocytopenia (15%) and anemia (15%). There were no treatment-related deaths.

Conclusions: Combination chemotherapy of irinotecan plus infusional cisplatin with rG-CSF support was well tolerated and effective in patients with advanced NSCLC.

1038 PUBLICATION

Second-line CPT-11 may improve survival in small cell lung cancer

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Background: We retrospectively analyze prgnosis factors of 134 patients with small cell lung cancer treated at our hospital between 1980 and 1997.

Methods: Case records that contained pretreatment parameters, treatmemet regimens, and survival information were collected. After univariate analysis, the multivariated evaluation of the impact of pretreatment parameters on survival was performed.

Results: Patients were divided into two groups according to initial treatment and second line treatmet: with/without platimun (n = 96/38), with/without CPT-11 (n = 36/82), respectively. The median survival times (MST) of all patients were 17.6 months for limited disease (LD) and 10.1 for extensive disease (ED). For the LD, the MST for those treated with platinum was 23.9 months, for those without platinum treatment was 8.3, showing a significant difference ($P < 0.01$). For ED, the MST of the group which received second-line CPT-11 was 14.7 months, for the group which did not receive CPT-11 was 7.8, showing a significant difference ($P < 0.05$).

Multivariate analysis was also performed to detect variables with significant influence on survival. According to this analysis, the significant prognostic variables were as follows; stage, performance status, lactate dehydrogenase, and second-line with CPT-11.

Conclusion: The improved survival time observed in small cell lung cancer patients treated with second line CPT-11 are notable, but because selection bias cannot be ruled out, the impact of second line CPT-11 on survival needs to be confirmed in prospective randomized trials.

1039 PUBLICATION

Vinorelbine (VNB) + ifosfamide (IFX) in non operable non small cell lung cancer (NSCLC). A phase II study

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Purpose: Though VNB plus Cisplatin (P) is the standard of care in non operable NSCLC, some patients (pts) have previous clinical conditions that increase neurotoxicity. An alternative is the replacement of P by IFX. VNB + IFX have been reported with response rate ranging 32–55%. A prospective multicentric confirmatory phase II trial have been performed at 11 institutions.

Methods: Between 1/96 and 9/98, 50 pts with non operable NSCLC were enrolled. Characteristics of population: median age 59 (r 36–65), male/female: 47/3. Number of metastatic sites: ≥3:18/50. Performance status ECOG 1–2 44/50. Stage IIIB/IV: 26/24. Schedule: VNB 30 mg/sqm IV day 1–8–15, IFX 2 g/sqm day 1 to 3, MESNA standard doses according IFX. Both drags each 28 days. Tumor assessment was done every 3 cycles and responses were confirmed 4 weeks later. Bronchoscopy was performed in complete responders.

Results: Response 43/50 are fully evaluable. CR: 1 PR: 13. Overall 33%. Toxicity (T): 221 cycles of VNB + IFX have been delivered [median 4 (r 2–10)]. T Grade$_{3-4}$ (WHO): leukopenia 13/50 trombocytopenia 1/50, alopecia 19/50, cardiotoxicity 1/50. There were no drug related deaths. Dose intensity: VNB 85% IFX 99%. Survival: median time to progression was: 5 months and median survival was: 9.5 months.

Conclusions: 1) VNB + IFX is an active regimen in non operable NSCLC. 2) T is manageable. 3) Replacement of P by IFX in VNB based chemotherapy seems to not affect survival.

1040 PUBLICATION

Carboplatin & gemcitabine in elderly patients with advanced non small cell lung cancer: Preliminary results

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Background: Thirty percent of non small cell carcinomas are diagnosed in patients (pts) over 70 years old. Carboplatin (CBDCA) seems the best tolerated platin in elderly pts. Gemcitabine (GEM) shows activity across lung cancer and tolerance in elderly pts. The aim of the study was to evaluate survival, response and tolerability in pts ≥70 years or younger but frail pts with advanced non small cell carcinoma (ANSCLC) treated with CBDCA & GEM.

Patients and Methods: Between May/1998 and Feb/1999, out 28 untreated ANSCLC entered the study, 25 have been up to now analyzed. Median age was 74 (range 65–81). ECOG performance status (PS) was 0/3 pts; 1/16 and 2/6 pts. Stage was IIIA/2 pts; IIIB/12 pts and IV/11 pts. Treatment consisted of: GEM 1250 mg/m^2 (1000 mg/m^2 in a first step with 6 pts) on day 1 & 8 and CBDCA (AUC = 4) on day 1, every 21 days. PS and symptomatology (pain, dyspnea, hemoptysis, anorexia and asthenia with a easy visual scale) were valuated before and after 3th & 6th cycles.

Results: We have up to now noticed a good tolerability though recruitment and treatment of pts is still ongoing. WHO myelotoxicity in the 62 cycles administered: thrombocytopenia grade I–II/4 & grade III/1; neutropenia grade I–II/19 & grade III/3 and anemia grade I–II/6 & grade III/2. No other major toxicities and no treatment related deaths were reported. At the time of the analysis, only 13 pts were evaluable for response: 5 had partial response/38.4%, 5 stable disease/38.4% and 3 progressed/23%. Up to now improvement in symptoms has been: pain 5/7, dyspnea 5/8, hemoptisis 3/3, anorexia 4/5 and asthenia 6/9.

Conclusions: This schedule shows good tolerability and appears effective in elderly pts with ANSCLC. Definitive results about response, toxicity, symptomatology and survival will be presented.