hematological or non-hematological toxicities. Only 1 patient had grade 3 thrombopenia; grade 3 anemia or neutropenia were not observed. Severe non hematological toxicity also was uncommon: grade 1-2 fatigue/asthenia in 27 patients (61%); grade 1-2 motor neuropathy in 26 (59%) and grade III in 4 (9%); grade 1-2 sensory neuropathy in 25 patients (57%); alopecia was mild.

Conclusion: Low-dose weekly paclitaxel regimen has good clinical efficacy with low toxicity in previously treated patients with advanced NSCLC, and may provide an additional treatment option for these population.

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A phase I/II study of weekly irinotecan combined with weekly cisplatin in patients with advanced non-small cell lung cancer

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Purpose: Synergistic effects between irinotecan and cisplatin have been reported. We had conducted a phase I trial combining these agents to determine the maximum-tolerated dose of weekly irinotecan plus weekly 20 mg/m2 cisplatin. Following a phase I study, we have conducted a phase II study to confirm the efficacy and safety of this combination therapy. Methods: For a phase I study, patients with advanced solid tumor, aged ≤ 75 years, performance status ≤ 2, and adequate organ functions were enrolled. They were treated at 4-week intervals using each dose of irinotecan plus fixed dose (20 mg/m2) of cisplatin on days 1, 8, and 15. The starting dose of irinotecan was 40 mg/m2 (level 1), and escalated in 10 mg/m2 increments until the maximum dose of 90 mg/m2 (level 6). In addition to severe toxicities, inability to complete the full-dose chemotherapy was considered as a dose limiting toxicity. After determining the recommended dose, a phase II study was conducted to previously untreated patients with non-small cell lung cancer (NSCLC). Results: In level 6 of a phase I study, dose limiting toxicities were observed in 3 of 9 patients (two for severe toxicities and one for inability to complete the initial two courses). Although the dose of irinotecan did not reach to the maximum-tolerated dose, the dose of irinotecan for the following phase II study was determined 90 mg/m2 according to the study design. For a phase II study, final goal is 100 patients. So far, 32 patients with advanced NSCLC were evaluated. All were assessable for toxicity and response. Response rates of NSCLC was 46% (13/32). Median response durations of NSCLC was 80 days. Total number of cycles administered was 95, and median number of cycles of NSCLC was 3. In 68 of 95 cycles (71.6%), anti-cancer agents were administered without skip. Dose reduction was performed in 25 cycles of 95 cycles. Toxicities were generally mild and reversible; toxicities over grade 3 were as follows; neutropenia (34.4%, 11/32), anemia (21.9%, 7/32), thrombocytopenia (3.1%, 1/32), diarrhea (25%, 8/32), anorexia (28.1%, 9/32), nausea and vomiting (18.8%, 6/32), abdominal pain (3.1%, 1/32). Conclusion: The recommended dose of irinotecan is 90 mg/m2 in the present study. The combination of weekly irinotecan and weekly cisplatin seems to be active against lung cancer

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The sequential administration of cisplatin-etoposide followed by topotecan in patients with extensive stage small cell lung cancer (SCLC). A multicenter phase II study

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We studied the sequential administration of topotecan after cisplatin-etoposide in patients with extensive stage SCLC.

Patients and Treatment: 38 patients with previously untreated extensive stage SCLC received 4 cycles of cisplatin 75 mg/m^2 IV on day 1 and etoposide 100 mg/m^2 IV on days 1–3 every 21 days followed by 4 cycles of topotecan 1.5 mg/m^2 IV on days 1–5 every 21 days. The median age was 63 and the performance status (WHO) was 0, 1 and 2 in 5, 25 and 8 patients, respectively.

Results: All patients were evaluable for toxicity and 32 for response. Overall 5 (16%) patients achieved CR and 15 (47%) PR for an overall response rate of 63% (95% c.i. 45.7–79.2). Among 19 patients achieving PR with cisplatin-etoposide, 4 (21%) achieved CR with topotecan. After a median follow up of 8 months, the median duration of response was 5 months, the time to tumor progression was 6.5 months and the probability of one-year survival was 37%. A total of 136 cycles of cisplatin-etoposide and 89 cycles of topotecan have been administered with a median number of cycles per patient 4 for each regimen. There were 2 toxic deaths after cisplatin-etoposide associated with grade IV febrile neutropenia. Treatment delays due to toxicity occurred in 17 cycles of cisplatin-etoposide and 20 cycles of topotecan while doses were reduced in 7 and 4 cycles, respectively. The incidence of grade 3–4 neutropenia, thrombocytopenia and febrile neutropenia was 24.5%, 2% and 3% after cisplatin-etoposide and 21%, 11% and 1% after topotecan. Non-hematologic toxicity was mild. The delivered dose intensity was 100% for cisplatin and etoposide and 82.5% for topotecan.

Conclusions: The sequential administration of cisplatin-etoposide followed by topotecan is a feasible and effective regimen in extensive stage SCLC.

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Chemotherapy with gemcitabine in elderly patients (or in patients not candidate for a cisplatin regimen) with advanced NSCLC: a multicenter phase II study

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Rationale: In a previous study we demonstrated in elderly patients with advanced NSCLC and in pts not candidate for a cisplatin regimen due to concomitant diseases or poor performance status that Gemcitabine administered at the dose of 1000 mg/sqm iv days. 1,8,15 every 28 is active and well tolerated (S.Ricci, Lung Cancer 2000). To improve the dose intensity of Gemcitabine and the compliance to the treatment we have performed a multicenter phase II study with the following schedule: Gemcitabine 1500 mg/sqm iv days 1,8 every 21 for 4 courses. The pts. with SD or OR after 4 courses of chemotherapy were randomized to receive futher 4 cycles of manteinance chemotherapy with Gemcitabine 1200 mg/mq iv days. 1,8 every 21 or best supportive care in order to evaluate the impact on TTP and OS. Patients characteristics: 110 patients were enrolled, 98 males and 12 females; median age 75 yrs range (50-84). PS: 0 = 42, 1 = 44, 2 = 22, 3 = 2; 30 pts. were adenocarcinoma., 53 squamous, 27 NSCLC.

Total number of cycles administered was 270 (median 4 cycles); we observed the following hematological and not hematological toxicity

	G1	G2	G3	G4
Neutropenia	0,7	2,6	0,7	–
Nausea/Vomiting	18,9	7,8	–	–
Thrombocytopenia	3,0	–	0,4	–
Diarrhoea	2,2	0,4	–	–
Anemia	15,6	3,0	0,7	–
Stomatitis	1,1	2,2	–	–
Skin Toxicity	1,1	–	–	–
Fever	8,9	2,2	–	–

Responses: up to now 88 patients are evaluable for response: 12 (13,6%) PR, 23 (26,1%) SID, 53 (60,2%) PD.

Conclusions: The Gemcitabine administered at the dose of 1500 mg/sqm iv days. 1,8 every 21 is active and well tolerated with a good compliance in elderly pts or in pts not candidate for a cisplatin regimen. The study is ongoing in order to evaluate the role of maintenance therapy.

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ZD0473 phase II monotherapy trial in second-line non-small cell lung cancer

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Aims: ZD0473 (cis-amminedichloro[2-methylpyridine]platinum [II]) is a new generation platinum drug designed to have an extended spectrum of antitumor activity and overcome platinum resistance mechanisms. A Phase II open-label, multicenter trial, was designed to assess the efficacy and tolerability of ZD0473 in patients with non-small cell lung cancer (NSCLC) who have failed previous platinum-based therapy.