therapy for superficial bladder cancer, except for the length of exposure. This study measures the toxicity of short GLA pulses on a cultured bladder cancer cell line and the tolerance of rat bladders to intravesical dosage.

Methods: a) The MGHU-1 anchorage dependent bladder cancer cell line was pulsed with meglumine-GLA (MeGLA) between 2 & 1000 μg/ml for up to 2 hours in 96-well plates. The MTT biomass assay was used to assess cytotoxicity 5 days later. b) Bladder histology was performed on rats given 0.3 ml, 2.5 mg/ml MeGLA intravesically. The drug was retained for 1&2 hours.

Results: Maximum cell kill was seen at drug exposures of 1 hour or more and over 125 mg/ml. Intravesical exposure to >10× this concentration of drug caused minimal histological damage, which resolved within two weeks.

Conclusion: GLA is toxic to bladder cancer cells given short exposures. It is well tolerated in an I nvivo model. A clinical application is feasible.

1139 PUBLICATION

Vinorelbine/gemcitabine in advanced non-small-cell lung cancer (NSCLC): A phase I trial

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Purpose: We performed a phase I dose-escalation trial of intravenous vinorelbine/gemcitabine in patients (pts) with advanced NSCLC.

Patients: Previously untreated pts (N = 33) were treated on days 1, 8 and 15. This cycle was repeated on day 29 (= day 1 of next cycle). Dose-limiting toxicity (DLT) was defined as severe myelotoxicity and/or any WHO Grade 3/4 non-hematologic toxicity.

Results: Toxicity for evaluable (2 cycles except in the case of DLT) pts and responses (CR+PR) for all entered pts are summarized below.

VIN mg/m²	GEM mg/m²	Eval.(all) pts	WBC WHO 3/4	DLT	CR+PR
10	600	3 (4)	0/0	0/3	0/4
15	800	3 (5)	0/0	0/3	0/5
20	800	3 (4)	0/0	0/3	0/4
20	1000	3 (3)	0/0	0/3	2/3
25	1000	6 (8)	4/0	1 cardiac/6	3/8
25	1200	3 (6)	2/0	1 pulmonary/3	1/6

Conclusion: The maximum tolerated dose has not been reached up to 25 mg/m² vinorelbine plus 1000 mg/m² gemcitabine.

1140 PUBLICATION

Phase I/II study of taxol/ifosfamide/cisplatin (TIP) combination chemotherapy (CMT) in advanced solid tumors (ST)

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In the present study, we evaluated the TIP combination in the outpatient setting in pts with a variety of advanced ST. Pts were entered into the following dose levels (DL); DL-I: T = 135 mg/m² day (d) 1-(1 hr), I = 2.25 g/m²/d d1–2 (total = 4.5), P = 40 mg/m²/d d1–2 (total = 80), DL-II: T = 175 d1, I = 2.25 d1–2, P = 40 d1–2, DL-III: T = 175 d1, I = 2.25 d1–2, P = 50 d1–2 (total = 100), DL-IV: T = 215 d1, I = 2.25 d1–2, P = 50 d1–2 and DL-V: T = 215 d1, I = 3.0 d1–2 (total = 6.0), P = 50 d1–2. G- or GM-CSF was given d5–14. 23 pts have entered: 5 at DL-I, 8 at DL-II, and 9 at DL-III. 1 pt with relapsed germ-cell tumor entered directly at DL-V to receive intensive P and I-based CMT. Histologies: 13 non-small cell lung (NSCLC), 6 ovarian (OC), 2 cervical Ca, 1 GCT, and 1 nasopharyngeal Ca. All but 5 had 2–8 cycles of prior CMT (no taxanes or I; P allowed) and progressed 6 wks after last CMT cycle. Characteristics: 13 males/10 females, age 25–67 yrs (median = 55), PS 0–2. The regimen was tolerated with outpatient administration in 15/23 pts. 21 pts are evaluable for toxicity. 1 pt died from PD prior to cycle 2. Toxicities; Gr 4 neutropenia for ≤5 days: 9 pts; 2 episodes of febrile neutropenia at DL-III and DL-V. Gr3/4 thrombocytopenia was seen in 8/2 pts. The MTD has not yet been reached. Pts are currently accrued at DL-IV and V. 9/21 PRs were seen (42%).

Conclusion: TIP combination appears to be feasible in the outpatient setting; phase II studies are planned in NSCLC, OC, etc, after the MTD is defined.

1141 PUBLICATION

Phase I dose finding study of irinotecan (CPT-11) over a short i.v. infusion combined with a fixed dose of 5-fluorouracil (5-FU) protracted continuous i.v. infusion in patients with advanced solid tumours

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Purpose: This ongoing Phase I study is designed to define an effective combination schedule of CPT-11 with 5-FU in patients with advanced adult solid tumours.

Methods: CPT11 is administered over a 90 min iv infusion on day 1 with a dose escalation schedule of 150, 175, 200, 250, 300 and 350 mg/m² q3w. 5-FU, in a fixed dose of 250 mg/m²/d, is administered as a protracted continuous iv infusion over 14 days, q3w. Pharmacokinetic (PK) parameters are also evaluated.

Results: Since June 1996, 16 patients were treated of whom 14 are evaluable for toxicity. Patients characteristics: median age 53 years (38–65); median PS 1 (0–2); sex: M/F 15/1; primary site: colorectal 5, oesophagus 2, head & neck 3, kidney 1, prostate 1, unknown primary 1, pancreas 1, small bowel 1, stomach 1. One partial response and various stabilisations were observed.

Dose (CPT11/5-FU)	N Patients.	N Cycles	Toxicity
Level 1: 150/250	3	10	No DLT
Level 2: 175/250	4	14	No DLT
Level 3: 200/250	3	7	No DLT
Level 4: 250/250	3	7	No DLT
Level 5: 300/250*	3(* 2 pts. too early)	3	Grade 4 Neutropaenia

Conclusion: Preliminary analysis shows this combination to be well tolerated. Study is ongoing, as maximum tolerated dose has not yet been reached at level 4.

1142 PUBLICATION

Abdominal and pelvic stop-flow (hypoxic, chemotherapeutic loco-regional treatment): Preliminary report of a phase I study

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Purpose: To establish the MTD, DLT and a safe dose for phase II study in stop-flow, a new loco-regional treatment with percutaneous double-ballon catheters, stop of blood flow and administration of high dose of Mitomycin-C (MMC) and Adriamicin (ADM), we started a phase I study.

Methods: From November 1995 to January 1997, were treated 23 patients, 8 pelvic and 15 abdominal, M/F 16/7, with histologically confirmed diagnosis of advanced neoplasms, unresectable or pretreated with standard chemotherapy. Dose escalation was: I° level MMC 15 mg/m² and ADM 75 mg/m²; II° level MMC 20 mg/m² and ADM 90 mg/m²; III° level Mit-C 25 mg/m² and ADM 120 mg/m².

Results: MTD and DLT were found both at III° level. Myelotoxicity grade IV was observed at III° level. Gastrointestinal toxicity grade III was reported at III° level. One patient had a reversible deep vein thrombosis, another patient had acute tubular necrosis reversed after 20 days. One case of paraparesis reversed after 4 days, was registered. No death related to procedure was reported. 5RP were observed in 10 pts evaluable. Accruitment is ongoing to establish the safe dose for phase II study.

Conclusions: Stop-Flow seems to be a new feasible and safe loco-regional treatment and the complete resolution of symptoms as pain encourages to continue this study and to promote a phase II study.