chemotherapy treatment with chi-square analysis. AM users visited church more frequent than non-users (p = 0.04). It was a borderline difference in the treatment intent (palliative vs adjuvant) of AM users in favor to palliative chemotherapy (65% of AM users vs 52% of non-users, p = 0.066). 38% of pts used one AM methods, 24% – two, 15% – three, 23% – more than three. 78% of AM users took herbs, 31% – pharmacological and biologic treatment, 19% – microelements, 11% – mind-body techniques, 10% – hunger-strike, 16% – other methods. 75% of AM users trusted to doctor for 100%, 16% for 80–90%, 7% for 50%, 1% – non trust, 2% – non answer. Only 45% of users reported to oncologist about use of AM.

Conclusions: Prevalence of real AM use is high (60%). Herbal remedies were the widespread AM methods. Medical oncologists need to be aware that about half of their patients may not tell them about AM use.

1130 PUBLICATION

Radiotherapy as a factor influencing psychological health of patients after breast conserving surgery (phase II)

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Purpose: Daily routine shows that anxiety and concern about radiotreatment is a factor with influence on psychological health of breast cancer patients. Beyond the description of data (phase I) aim of phase II was to identify possible influencing factors on psychological health and to find correlations and interactions between these factors based on a higher quantity of patients.

Patients and Method: 111 Patients participated in the phase II (age 33–84). They received two questionnaires (first and last day of radiotherapy) asking for coping strategies, psycological burden and side effects as well as surrounding factors like medical staff and rooms. Statistically significant correlations between identified factors were identified using t-test.

Results: The question for anxiety regarding radiotherapy allows to identify patients with a high level of treatment-related psychological burden. Patients with a low level of anxiety are significantly less concerned about expected negative effects on breast cosmesis and side effects and feel better informed than patients with high anxiety level. Also perception of treatment facilities (waiting room and treatment room) was significantly more positive.

Conclusions: Our results give evidence that patients with high treatment related anxiety require special attention. This underlines the importance of our phase I-result that the relation to the medical staff is an important factor in regard to reduction of treatment related psychological burden.

1131 PUBLICATION

Quality of life in patients with breast cancer: A psychosocial investigation

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Purpose: To investigate on psychosocial problems of patients with breast cancer in Iran.

Methods: A hospital-based prospective study was conducted to collect data on psychosocial problems in women with breast cancer. During one year 169 breast cancer patients were identified and three months after their initial treatments they were invited to take part in the study. A 42-item questionnaire containing items on study objectives was used to collect data.

Results: Out of 169 breast cancer patients, 152 (90%) agreed to be interviewed. The mean age was 47 (SD = 13.4) years, the majority were married (69%) and underwent the modified radical mastectomy (83%). The main findings indicated that the majority of patients had trouble doing strenuous activities (84%), had pain in their arms and shoulders (68%), felt tense (59%), were worried (68%), felt irritable (72%), were worried about their health in the future (98%), and 43% of patients said that their pysical condition and medical treatment interfered with their social life. In addition, it was found that 49% of patients had sever anxiety and 22% had sever depression symptoms.

Conclusion: The findings of this first study of the quality of life in patients with breast cancer in Iran is very alerting. It seems that to improve quality of life in this group of patients there is an urgent need to recognise the problem and provide a comprehensive cancer sevice for carring breast cancer patients in Iran.

1132 PUBLICATION

Medical treatment acceptance related to psychotherapeutical support of the oncologic patient

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Introduction: the psychological background of patients with cancer has been a research topic by the authors for many years. A retrospective study analyzing medical records from oncologic patients was made to evaluate whether the psychotherapeutical support modifies somehow the medical treatment acceptance.

Patients and Methods: 52 records from patients with solid tumors, ranging in age from 35 through 65, were evaluated in a case-control study. The medical treatment acceptance was compared between patients with any kind of psychotherapeutical support (i.e. familial and individual assessment with a minimum of 20 sessions) and those with no emotional aid at all.

Results: the acceptance and adhesion to medical treatment (i.e. chemotherapy, radiotherapy) was significantly better (chi square = 8.51 p = 0.0039) among patients who were helped to build a strong psychological background.

Conclusions: outstanding efforts are made every moment in order to defeat cancer. Out of these efforts, only a small part is dedicated to understanding the emotional aspects of the disease. The authors conclude that these aspects play a big role in its evolution and should be paid greater attention, not only for academical purposes but also for the patient's benefit.

1133 PUBLICATION

Information an education programmes on breast cancer. The NCI of Naples experience

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The information and education programmes on breast cancer of the NCI of Naples are addressed both to healthy and affected by cancer women. We monthly organise series of lessons on breast diseases and the breast self-exam for the healthy women. 1002 women participated to these meetings in the last three years. Data about the psychological impact caused by these meetings on cancer early detection showed that only 3.8% didn't prefer to know, while 96.2% was more confident after the meeting. 76% of the interviewed women didn't practice the breast self-exam because of the fear and the lack of knowledge about the breast self-exam and how to do. Our Institute provides a pre- and post-operating counselling for the patients. During the pre-operating counselling the patients get to know the diagnosis and the therapeutic options in order to give the informed consent. The past-operating counselling provides a single or in groups meeting soon after the operation and another, after the hospital dismissal, with the COMITES constituted by a surgeon, an oncologist, a radiotherapist, a psychologist and one or more health operators. During this meeting the adjuvant treatment following to the result of the histological exam are communicated to the patient and his relatives. According to our experience the use of this procedure is positive infact thanks to the patient feeling that all the equipe is looking after him, there is an increase (about 45%) of the compliance to the medical treatment.

Clinical pharmacology

1134 ORAL

A phase I trial of SU5416 a novel angiogenesis inhibitor in solid tumours, incorporating MRI assessment of vascular permeability

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SU5416 (Z-3-[(2,4-dimethylpyrrol-5-yl)methyldenyl]-2-indolinone) is a potent inhibitor of vascular endothelial growth factor receptor signalling. In rodent xenografts treatment with SU5416 led to reduction in tumour growth

rate and decreased vascularisation. In this Phase I trial we have explored the toxicity and pharmacokinetics (PK) of this compound, and attempted to assess its impact on the vascular permeability of solid tumours using Magnevist® enhanced MRI. Escalating doses of SU5416 were administered to sequential cohorts of three patients twice weekly for four weeks per cycle to a maximum of three cycles. To date 11 pts (8 F:3 M), median age 47 (R 25–74) have received 22 cycles of SU5416 at the following doses: 48 mg/m^2 (3), 65 (3), 85 (3), 110 (2). No dose limiting toxicity has been observed. Mild local venous irritation and phlebitis were common (10/11 pts). Despite premedication, hypersensitivity reactions (attributed to the diluent Cremophor™) requiring additional steroid administration have been observed in 4 pts but treatment was continued in all. Other toxicities were mild to moderate and appeared dose related: fatigue (4/11), headache (4/11) and emesis (4/11). No haematologic or metabolic toxicity has been observed. PK of the parent drug in the first 9 patients showed that clearance was rapid (mean 74.3 l/hr, SD 29.5 l/hr) and there was a trend towards an increase in drug clearance with repeated administration. No responses have been seen yet, however 4 pts have had disease stabilisation. At the doses reached no impact on vascular permeability has been visualised by contrast enhanced MRI performed one hour after infusion of SU 5416 and further studies will be performed at 4 hours. Accrual is ongoing.

1135 ORAL

Phase I trials with ET-743, a marine derived (MD) anticancer agent

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ET-743 is a novel MD compound, minor groove binder-selective for G rich sequences, that is completing the phase I evaluation. Five different infusion times (drug given every 3 weeks) have been tested and mature data in 171 patients (pt)/424 cycles are now available

	1 h iv	3 h iv	24 h iv	D × 5	72 h iv
No. Pt	40	19	52	41	19
MTD* 1100	1800	1800	1900	1200	
RD	1000	NA	1500	1650	NA

* = mcg/m^2; NA = not available yet; MTD = maximal tolerable dose; RD = recomended dose.

The dose limiting toxicities are hematological tox and fatigue. As expected from the preclinical tox, drag induced changes in the liver function test have been consistently reported. ET-743 induced transaminitis has an early onset, peaks by day 3–4 post drug administration, a median time to baseline values (AST/ALT) = 10 days and lacks a cumulative effect. Clear evidence of activity has been seen in patients with advanced resistant sarcomas, breast, melanoma and mesothelioma. PKs of ET-743 fit with a bicompartimental model. AUC values achieved in patients are within the range of the figures obtained at curative doses in nude mice bearing tumors. Early phase II studies incorporating 1500 mcg/m^2 iv-24 hours infusion/3 weeks are underway.

1136 ORAL

NCIC CTG IND 113: Two phase I dose escalation pharmacokinetic (PK) studies of BAY 12-9566 (BAY) in combination with either doxorubicin (DOX) or modulated 5-fluorouracil (FU)

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Rationale: BAY 12-9566 is a non-peptidic selective inhibitor of MMPs 2 and 9.

Methods: Two parallel dose escalation studies with a cross-over design were conducted. In cycle (C) one, patients (pts) received chemotherapy (CT) alone and in C2 CT plus BAY. BAY was to be given in a fixed dose of 800 mg bid; FU starting dose was 350 mg/m^2 daily × 5 with a fixed dose of leucovorin 20 mg/m^2 (arm A); DOX starting dose was 50 mg/m^2 (arm B). Dose limiting toxicity (DLT) included grade 3/4 toxicity.

Results: 23 patients (pts) have been accrued: median age was 60 yrs (44–78); 12 pts were female; performance status was 0 (5 pts), 1 (13 pts), or 2 (5 pts). Tumor type included colon (6 pts), ovary (4 pts), NSCLC (3 pts), renal (2 pts); 14 pts had had prior CT and 11 prior radiation; common sites of disease included: lung (15 pts); nodes (11 pts); liver (11 pts). Arm A: 12 pts have been accrued to 2 dose levels (DL); at DL-1 (FU 350 mg/m^2 plus BAY 800 mg bid po) thrombocytopenia was dose limiting, although PK in C2 was similar to C1; in DL-2 pts were treated with FU 350 mg/m^2 plus BAY 400 mg bid po without DLT; dose escalation continues in DL-3 (FU 400 mg/m^2 plus BAY 400 mg bid po). Arm B: 11 pts were accrued to 3 DLs. DL-2 (DOX 60 mg/m^2 plus BAY 800 mg bid po) was well tolerated although PK revealed a 30–40% increase in DOX levels in C2 compared to C1. At DL-3 (DOX 70 mg/m^2 plus BAY 800 mg bid po) DLT attributable to DOX was seen; toxicity was similar in C2 and C1 with no evidence of an interaction.

Conclusions: There appears to be evidence of a pharmacodynamic (thrombocytopenia) though not a PK interaction with BAY and FU, although with reduction of BAY to 400 mg bid po the combination was tolerated. Dose escalation in Arm A continues. Despite modest evidence of a PK interaction in Arm B, full dose BAY (800 mg bid po) can be safely administered with DOX 60 mg/m^2 and is recommended as the dose for further study.

1137 ORAL

Phase I dose escalation, pharmacokinetic (pk) study of a novel vascular endothelial growth factor (VEGF) receptor inhibitor, PTK787/ZK 222584 (PTK/ZK)

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PTK/ZK is a novel, low molecular weight, orally bioavailable compound that is a potent inhibitor of VEGF receptor tyrosine kinases. In vitro, it inhibits VEGF-mediated signal transduction and endothelial cell functional responses. After oral dosing in rodent models, it inhibits VEGF-mediated angiogenesis, tumor vascularization, and tumor growth. Preliminary data from a Phase I trial in advanced cancer patients are available. Cohorts of 3 patients were treated at dose levels of 150, 300, 500 and 750 mg once daily for 28 days. Dose escalation is continuing. Patients have been treated for up to 4 cycles without dose interruption or delay. No dose limiting toxicity, hematologic or hepatic toxicity was observed. Pk and surrogate marker samples were obtained at multiple times on days 1, 15 and 28 for each dose level. Current data indicate PTK/ZK is rapidly absorbed, with a Tmax of 1.1–2.0 hours, an average terminal half life (t1/2) of 4.5 hours and has no evidence of accumulation following once daily dosing. The average AUC values decreased slightly from day 1 to day 15 at all dose levels. The mean AUC (0-infinity) was proportional to the administered dose for all dose levels studied. PTK/ZK is well tolerated with a favorable pk profile and can be administered on a continuous basis. This novel compound has therapeutic potential for the treatment of solid tumors and other diseases where angiogenesis plays an important role.

1138 ORAL

Phase I dose finding study with irinotecan (CPT-11) in cancer patients (pts) with hepatic dysfynction

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Biotransformation pathway of CPT-11, and especially enzymes which convert CPT-11 into its active metabolite SN-38, are mainly located in liver. Thus, hepatic dysfunction could alter CPT-11 pharmacokinetic (PK) and may increase the risk of toxicity. This study was designed to determine the maximal tolerated dose and to investigate the PK of CPT-11 in pts with liver dysfunction. Pts groups (gr) were based on the initial total bilirubin level (Tbili): gr A (≤1.0 Normal Limit-NL) and B (>1.0 to ≤1.5 NL) with 350 mg/m^2 starting dose given every 3 weeks. In gr C (>1.5 to ≤3.0 NL), 3 dose levels were planned: 175-240-350 mg/m^2. Transaminase level was ≤20 NL in all gr. Doses were adjusted in pts who experienced Tbili modifications or dose-limiting toxicity (DLT). Blood was sampled up to 24 h post infusion for PK evaluation. Twenty-two pts were treated (M/F: 15/7, median age: 53, PS 0–2): 7 pts-26 cycles (cy), 4 pts-14 cy, 6 pts-16 cy and 5 pts-20 cy so far in gr A, B, C at 175 and C at 240 mg/m^2, respectively. DLTs observed at 1st cy: 1/7 pts-gr A (grade 4 febrile neutropenia-FNG4), 1/4 pts-gr B (FNG4), 1/6 pts-gr C (FNG4) at 175 mg/m^2 and 3/5 pts-gr C (grade 4 diarrhea-thrombocytopenia, FNG4) at 240 mg/m^2. Preliminary PK parameters, obtained by