when research protocols are designed. Clinical research is a team effort of multidisciplinary experts and appropriate end-points must be carefully chosen with adequate balance between benefits and risks for trial subjects. International large scale conclusive multicenter trials are necessary to detect small but medically important differences. Statistical methodology is essential to ensure ethics in cancer clinical trials and the involvement of statisticians should be promoted for all ethical reviews to avoid ill conceived trials being approved. It is also counterproductive to require ethical review from each individual institution. Rapid protocol review and activation is essential for early dissemination of breakthrough therapeutic advances. The French system with a central review facilitates activation of trials and should be considered for other E.U. countries. Specific guidelines should be developed on the European level for ethical review dedicated to oncology.

881 POSTER

COULD ANTINEOPLASTIC THERAPY INTEGRATE PALLIATIVE CARE FOR SYMPTOM RELIEF IN ADVANCED/REFRACTORY CANCER PATIENTS?

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Purpose: 1) to offer continuity of care and in- and outpatients services to far-advanced end stage cancer patients, bridged by double employment of the same oncology/palliative care physicians and nurses; 2) to integrate a patient-tailored anticancer treatment to supportive and palliative care for relieving disease-related distressing symptoms on account of patients' expressed needs and wishes.

Patients: 86 patients suffering from active, progressive far-advanced cancer: refractory NHL: 7; AIDS-related-NHL: 1; CML in blast crisis: 3; elderly AML patients with resistant disease: 9; lung: 18; gastrointestinal: 23; renal: 1; urinary tract: 6, head and neck: 4; metastatic breast: 2; ovarian carcinomatosis: 7; melanoma: 1; unknown primary: 4.

Methods: 1) **Different options for setting** were offered by the same multidisciplinary team: 1) traditional hospital setting; 2) continuous home-care; 3) hospitalization at home. 2) **Anticancer chemotherapy**: low dose reduced-toxicity different regimens have been proposed to patients with chemoresponsive tumour with the only objective of the symptoms relief. Adequate supportive therapy, transfusional and antimicrobial, has been provided to hematological pts at home. 3) **Palliative medicine** was given to all the patients for the control of symptoms and for terminal illness, both in hospital and at home.

Results: 55 patients (62%) agreed to receive palliative chemotherapy (38 in hospital, 17 at home). A symptomatical response rate of 64% has been achieved. Patients receiving no anticancer treatment experienced comparable symptoms but a higher grade of distress (in one or more of the items of Symptom Distress Scale) to those patients who were on palliative chemotherapy. In our opinion the value of symptomatic response achieved with chemotherapy should not be decried and a more close integration between oncologists and palliative care teams could prove fair for patients.

882 POSTER

LOCAL TUMOR CONTROL WITH MICROWAVE HYPERTHERMIA (MWHT) IN ADVANCED TUMOR DISEASE

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Local tumor control is considered worthwhile in patients with advanced malignant disease to improve quality of life, though there is no effect on survival. MWHT in combination with radiotherapy or chemotherapy is able to improve remission rates of radiation and chemotherapy alone significantly. Between August 1990 and March 1995 we treated 31 patients with MWHT (tumor temp, higher than 41.5 dgr. C for 1 hour in 4 to 8 treatment sessions) additional to radiation or chemotherapy. Recurrent malignant melanoma (18), locoregional recurrence of breast cancer (5), pelvine recurrence of rectal cancer (6) and recurrent retroperitoneal sarcoma (2) were the indications. The rate of complete local response was 45%, partial remission we saw in 42%, no change in 13%. The rate of treatment related side effects was low and we can conclude that MWHT in combination with radiation or chemotherapy is an effective and safe treatment for local control of advanced malignant disease.

883 POSTER

MULTISTAGE CARCINOGENESIS ANALYZED FROM CANCER INCIDENCE RATES

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Carcinogenesis is a multistage process driven by genetic damage and epigenetic changes. The classic view of two-stage carcinogenesis, in which tumor initiation (mutation) is followed by tumor promotion (epigenetic changes), has been conceptually important but is too simplistic. There may be six or more independent mutational events. Average annual age-specific cancer incidence rates from 1981 to 1985 reported by the SEER program are analyzed, and interpreted in accordance with a mathematical model which takes into consideration the number of events needed for tumor generation (n) and annual probability of occurrence of that event (p). Basically, cancer incidence rates are equated in terms of time as $(1-(1-p)^t)^n$. A genetic algorithm is used to find the minimum sum of squares. Overall, 4 to 8 events occur with an annual probability of 0.006 to 0.01. Specific data by site will be presented in tabular and graphical form.

884 POSTER

ONCE A DAY (I.E. 24 HOURLY) KAPANOL™, A NEW SUSTAINED RELEASE MORPHINE FORMULATION, IN THE TREATMENT OF CANCER PAIN: MORPHINE METABOLITE PROFILES

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The role of the morphine metabolites, morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G) in the analgesia observed following morphine administration is controversial. There is greater acceptance of the analgesic role ascribed to M6G while M3G is alternatively considered to be inactive or result in functional antagonism. Kapanol™/Kadian™ (Glaxo/Faulding) is a new sustained release morphine formulation consisting of polymer coated pellets in a capsule. Twenty-four patients completed a randomized, double-blind, two period, crossover study comparing 24 hourly Kapanol to 12 hourly MS Contin. The morphine metabolite profile was determined in a randomly selected subset of those patients (n = 8). The Cmax, Cmin, AUC, time that the plasma morphine concentration was $\geqslant$0.75 Cmax (for that metabolite) and fluctuations in plasma morphine concentrations were not significantly different ($P > 0.05$, repeated measures ANOVA) between the two formulations for either metabolite. However, the Tmax for both M6G ($P < 0.001$) and M3G ($P < 0.05$) was significantly longer following Kapanol administration compared to MS Contin. We conclude that the plasma metabolite profiles are very similar to the respective morphine profiles. Therefore, the release characteristics of morphine from the formulation has a major influence on the morphine metabolite profiles.

885 POSTER

COCHRANE CANCER NETWORK

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The Cochrane Collaboration was founded in 1992 to prepare, maintain and disseminate systematic reviews of all forms of health care and to establish a reliable register of randomized controlled trials (RCTs). Since then the Collaboration has grown rapidly. The first edition of the database of systematic reviews was released earlier this year and the number of RCTs that can be easily identified within Medline has been doubled. Although cancer has a long history of RCTs and of quantitative systematic reviews (meta-analyses), many unresolved questions concerning its prevention, diagnosis and treatment remain. A Cochrane Cancer Network is being set up, therefore, to encourage the conduct of systematic reviews and to coordinate their input to this important initiative. The Network will provide a framework for convening exploratory meetings of people interested in forming collaborative review groups to tackle particular aspects of cancer care. Such international groups should contain members from a variety of disciplines and must be willing to collaborate in the preparation and updating of systematic reviews of all relevant trials which fall within the agreed scope of that group. The Network will help and encourage the training of both writers and users of systematic reviews, including providing guidance for reviewers who