

lower than in earlier monoinstit. trials and reached only 5% (12% DS) in 42 non-eligible P. The responsibility of the treating oncologist for his P's quality adjusted life months is stressed.

892 POSTER TOTALLY IMPLANTABLE VENOUS ACCESS DEVICES (TIVAD) IN CANCEROLOGY. RESULTS OF 141 PERCUTANEOUS CANNULATION

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Introduction: cytotoxic chemotherapy often requires a central venous access by a catheter or a TIVAD.

Materials: we reviewed a homogenous series of 141 patients: 87 women, 54 men, ranging in age from 20 to 80 years old (mean age 54 years). Each patient had a malignant disease, most frequently being metastasis: breast cancer (41.8%), head and neck cancer (10%), ovary cancer (7.8%), lung cancer (7%), sarcoma (5.6%) colon cancer (4.2%) and others (23.4%). The TIVAD used was the standard model Districath® (Districlass) for 90% cases, joined by a silicon catheter with an internal diameter of 1.10 mm.

Methods: after a prophylactic antibiotherapy, a neuroanalgesia and a local anesthetic, firstly we used the method of percutaneous cannulation of the subclavian vein and then implanted the TIVAD 2 cm under the clavicle. All implantations were made under normal sterile surgical procedures. The treatment started after 4 days and injection of heparin continued every 29 days.

Results: percutaneous venous access was successful 139 times (98.6%) with the puncture 112 times (79.4%) on the right. We regret having punctured the subclavian artery 6 times (4.2%) but this did not cause any after-effects. However we experienced no complications of haematoma, pneumothorax, local infections or septicemia. Unfortunately we had to remove 7 TIVADs due to 3 ruptures of the catheter, 2 septicemias, 1 case of ulcerated skin and 1 for psychological intolerance. The time patients spent in the operating theatre in 68% of the cases ranged between 1.5-2 hours. During this study in 1994 we did not experience any extravasation of the cytotoxic drug and no catheter blockage, nor any TIVAD related deaths.

Conclusion: in our series, the implantation of TIVAD by a percutaneous puncture of the subclavian vein is a quick, reliable method with a low morbidity rate. This operation can lead to many potential complications and should be carried out stringently in surgical conditions. Nevertheless we believe that the percutaneous puncture method provides good venous access and improves the security and the quality of patient life.

893 POSTER ADVANTAGES OF THE COMPUTER PROGRAM "HEM" IN FOLLOWING, PROCESSING AND ANALYZING DATA OF CHEMOTHERAPY TRIALS

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One of the most difficult stages in clinical drug trials is collecting, selecting and analyzing data. In the past, this was done manually, which took almost 80% of investigation's time, and the possibility of the mistakes was very high. Computer program "HEM" has been developed and used for storage and processing data in clinical trials. Program has three independent parts: data entry, data processing and data entry control. Data entry includes entering: data about patient's illness before the therapy (diagnosis, TNM classification, stage, PH diagnosis, previous therapy, performance status (PS), localization and dimension (L&D) of the primary tumor or local recurrence, L&D of the metastases), during and after the chemotherapy (PS, L&D of the primary tumor or local recurrence, L&D of the metastases and therapy toxicity-WHO classification), as well as the data about patients excluded from the trial. The initial date, data concerning therapy effect, data concerning therapy toxicity and dose intensity were analyzed for each optionally defined groups, by using data processing. All combinations of initial data could be used for defining these group. Data accuracy is assessed with data entry control. Advantages of "HEM": 1) reduction of the time necessary for data entry and analyzing data—used time is less than 10 min. for all entries per patient, and 30 min. per complete trial data analyzing, 2) logical control minimizes mistakes (incomplete, wrong and missing data), 3) lost data are eliminated with daily "back up", 4) daily follow up is enabled by data

entry control, 5) it improves accessibility of the data. "HEM" was made in Clipper, installed on PC computer and is user friendly oriented program. It was installed in Sept. 1991. Today, about 1200 patient's records in 30 clinical trials are followed with "HEM".

894 POSTER THE PALLIATIVE TREATMENT OF THE SOLITARY BRAIN METASTASES WITH THE LEKSELL GAMMA KNIFE STEREOTACTIC IRRADIATION

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From November 1992 to May 1995 there were 75 patients with 112 intracerebral metastases treated in Hospital Na Homolce in Stereotactic and Radiation Neurosurgery Department. The study characterises the most optimal group of solitary brain metastases indicated for Leksell Gamma Knife treatment, which is mainly determined by volumes up to 20 cm³, location in the brain hemispheres, proper histological type, Karnofsky rate 70% and more, age under 60 years and with no other organ generation (except CNS). For evaluation of late effects longer time interval (min. 18 months from the treatment) will be needed. However, the prognostic factors, symptomatic response, local control, acute toxicity and quality of patient's survival can be evaluated. The main advantages of the described method are already apparent now: no operation mortality, minimal morbidity, short hospital stay and nearly no claims to change of patient's way of life. The stereotactic radiosurgery and radiotherapy fulfil the requirements of palliative treatment: maximum benefit with minimal treatment and investigation procedures.

895 POSTER PATIENT PREFERENCE OF ANTIEMETIC TREATMENT: A PLACEBO CONTROLLED, DOUBLE BLIND COMPARISON OF GRANISETRON WITH GRANISETRON PLUS DEXAMETHASONE

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The antiemetic efficacy of 3 mg *iv* granisetron (G) was compared with G plus 20 mg *iv* dexamethasone (Dex) in a double blind placebo (Plac) controlled cross over study. Seventy-two patients (pts) undergoing moderate to highly emetogenic chemotherapy (C), received both antiemetic treatments. At the end of the study, before the study was unblinded, all pts were asked to state their preference of antiemetic treatment; either first cycle, second cycle or no preference (NP). The results are shown below.

	Patient Preference (No. Pts)		
	G + Dex	G + Plac	NP
Sequence: cycle 1/cycle 2.			
G + Dex/G + Plac	13	8	18
G + Plac/G + Dex	16	6	11
Combined	29	14	29

An analysis of the patient preferences (PP) showed that there was a significant difference ($P < 0.022$, Likelihood Ratio Chi Sq.) between the preferred treatments. The 24 hour complete response rates (no vomiting or retching and only up to mild nausea) for combined cycles were as follows; 80.6%, for G + Dex and 65.3% for G + Plac ($P = 0.015$).

Overall, more pts (29) preferred the antiemetic session where Dex was incorporated with G than with the G + Plac (14 pts). These data show that PP may be an additional sensitive means of evaluating antiemetic efficacy in cross over comparator studies and may be influenced by the level of control of acute emesis.

896 PUBLICATION PHOTODYNAMIC THERAPY OF TUMOURS: NEW ADVANCES

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Studies on transport of HpD by high and low density proteins (VLDL, LDL and HDL) have suggested that apparently lipoproteins possess two

classes of binding sites for Hp which are probably located in the apoprotein matrix and the lipid core, respectively. Lipoproteins play an important role in the transport of haematoporphyrins (Hp and HpD) in the bloodstream, it has been suggested that tumor localising property of the porphyrin photosensitisers used in photodynamic therapy (PDT) is related to such binding, particularly to low lipoprotein.

LDL binds to specific receptors on cellular membranes by arginyl and lysyl residues. Chemical modification of these residues abolishes the interaction between lipoproteins and receptors both *in vitro* and *in vivo*. *In vitro* studies have also demonstrated that tumors have a higher affinity binding for LDL because of an increase of the number of membrane LDL-receptors. To a greater understanding of transport mechanism of porphyrins we have studied the affinity of HpD to proteic amino acid by thin layer chromatography and nuclear magnetic resonance (NMR), using a standard mixture. Our results indicate that the tryptophane is the aminoacid mainly involved in HpD binding. Whereas other aromatic aminoacids are at secondary levels. Furthermore a study on the binding sites of human serum albumin to HpD by NMR is also presented. A better knowledge of these binding sites will allow to improve photodynamic therapy and to transfer selectively antitlastic chemo therapeutic drugs in neoplastic cells.

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PUBLICATION

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

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Sustained release morphine formulations are now generally accepted as the formulations of choice in the treatment of severe cancer pain. Kapanol™/Kadian™ (Glaxo/Faulding), a new sustained release formulation consisting of polymer coated pellets in a capsule, has recently

been shown to have a superior morphine release profile compared to the standard tablet, MS Contin. In fact, the release characteristics of morphine from Kapanol suggested the possibility that one oral dose of Kapanol per 24 hours could effectively treat severe cancer pain. Twenty four patients completed a randomised, double-blind, two period, crossover study comparing 24-hourly Kapanol to 12-hourly MS Contin. The morphine dose per 24 hours was identical for the two formulations and morphine pharmacokinetics were determined over 24 hours at steady state for each formulation (i.e. after 7 days). The C_{max}, C_{min}, AUC and fluctuations in plasma morphine concentrations were not significantly different between the two formulations ($P > 0.05$, repeated measures ANOVA). Kapanol had significantly longer T_{max} values ($P < 0.001$) than MS Contin. These results indicate that one Kapanol dog per 24 hours should at least be as efficacious as 12 hourly MS Contin in the treatment of severe cancer pain from the pharmacokinetic perspective.

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PUBLICATION

PALLIATIVE SINGLE-DOSE THIRD-BODY IRRADIATION OF MULTIPLE METASTASES IN TERMINALLY ILL PATIENTS

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In the group of 34 patients (pt) with multiple bone, lymph-nodes and visceral metastases 44 third-body (ThB) areas were irradiated using 600 cGy to the upper ThB and 1000 cGy to the middle ThB. The most of pt were terminally ill. Within the group 27 pt (80%) were III° or IV° of physical activity WHO (Zubrod) scale.

The result of the treatment was either fast relief of pain (40% doing so within 24–48 h.) as well as change to more active physical state. WHO scale III° or IV° were 17 pt (50%) according to 27 (80%) before ThB irradiation. All pt were hospitalised and were discharged typically one day after ThB irradiation. No deaths were seen immediately.

The method seemed to improve quality of life in about 40% of pt, not duration of life.

Testicular tumours

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ORAL

VARIATIONS IN CANCER SURVIVAL: A QUALITY ASSURANCE CHALLENGE

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Published survival figures for cancer indicate significant variations across Europe. Much of this variation may be due to different cancer registration practises and it is notable that two European countries, Denmark and Scotland, which have effective population based cancer registries, apparently low five year survivals for a range cancer.

Recent changes in the way health care is administered within the United Kingdom have made it possible to examine in detail variations in clinical practice. It is clear that much of the variation in outcome is related to differences in standards of clinical care. Clinician and centre specific outcome following treatment for testicular teratoma, melanoma, breast cancer and colon cancer have been reviewed. For these cancers some hospitals are no longer recognised as providing effective treatment and for the commoner cancers, individual clinicians have been accredited within hospitals.

Further work on the cost-effectiveness of various interventions has been done which has resulted in the Health Authority restricting the development of new services such as a screening for prostate cancer. Progress towards the delivery of cancer care on sound research evidence will be described.

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ORAL

ESTROGEN RELATED CANCER RISK IN MOTHERS OF TESTICULAR CANCER PATIENTS

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The belief that estrogens are centrally involved in the pathogenesis of both testicular cancer in young men and cancers in the endometrium and female breast has become widespread. In order to provide further insight into the possible hormonal links between these cancers, we investigated the cancer pattern in a large cohort of women who had given birth to sons who developed testicular cancer. Particular focus was given to estrogen-related cancers.

Material: Mothers of 2,204 testicular cancer patients were identified, with a total of 70,063 person years of follow up.

Results: No increased risk was found with regard to breast, endometrial or ovarian cancers among mothers of testicular cancer patients. Brothers of testicular cancer patients have a significantly increased relative risk of developing testicular cancer ($P < 0.001$).

Conclusion: On the basis of this large study no clues of common hormonal etiology of testicular cancer in young men and cancers of the endometrium and breast could be identified. Some kind of hereditary predisposition of testicular cancer seems likely.