

with IDIFO ( $9 \text{ g/m}^2/\text{cycle}$ ) and our administration modality (1 hour instead of C.I.V.) may account for the 50% decrease of AUC and half life between the 1st and 3rd treatment days observed in our pharmacokinetic study (Lokiec *et al.* ASCO 95).

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PUBLICATION

### EMBRYONAL RHABDOMYOSARCOMA (ERMS) IN ADULTS: RESULTS OF TREATMENT

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Many studies suggest that adults patients (p) who develop a so-called pediatric cancer have a worse prognosis than do children. We have reviewed 7 adult p with ERMS, that we treated between Dec 1975–March 1991. Diagnostic was done by surgical biopsy in all cases. Age range was 16–42 years, mean 26.6. All p were males. All p underwent surgery. The distribution (G, IRS-1) was: GI three p (42.8%), GII one p (14.3%),

GIII two p (28.6%), GIV one p (14.3%). Primary sites were genitourinary tract in 5 p, 71.4%, parameningeal, in maxillary-ethmoid sinus, 1 p, 14.3%, and chest wall, 1 p (14.3%). Radiation therapy was delivered in 5 p, with a dose range of 40–55 Gy; volume ranged from tumor bed to inverted Y. All p received chemotherapy. CYVADIC was given to two p. The others programs were VAC, vincristine plus doxorubicin (D) and cyclophosphamide, ifosfamide (I) and etoposide, I plus dactinomycin plus D. The p with parameningeal site received intrathecal methotrexate. Six p (85.7%) suffered progressive disease. Time to progression was  $4.5 \pm 2.16$  months (median and SD). Metastatic sites involved lung (2 p), lung and bone (2 p), meninges (1 p) and lung, liver, soft tissues and brain (1 p). The actuarial 3-year survival (Kaplan-Meier) was 16.7%. Median survival was 9 months. Only 1 p was alive and disease-free after 38 months of follow-up. This report suggests that adults with embryonal rhabdomyosarcoma have a worse prognosis than children. Further improvements in our knowledge of biology of RMS and new therapeutic strategies are needed.

## Palliative treatment

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### KADIAN<sup>TM</sup>/KAPANOL<sup>TM</sup>—A ONCE DAILY MORPHINE FORMULATION

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Although oral morphine remains the opioid of choice for the management of moderate to severe cancer pain, controlled-release morphine formulations have only enabled dosing every 8 to 12 hours. Kadian<sup>TM</sup>/Kapanol<sup>TM</sup> (K) is novel polymer-coated morphine sulfate pellets (20, 50, 100 mg) in a capsule designed for 12 to 24 hourly dosing. This randomized, double-blind, double-dummy, parallel group study compared the efficacy and safety of K q12h or q24h to MS Conlin<sup>®</sup> tablets (MSC) q12h. Eligible patients with cancer pain were titrated to adequate analgesia with a stable dose of immediate-release morphine sulfate (IRMS) over a 3 to 14 day lead-in, then randomized to one of the three treatments for  $7 \pm 1$  days. Rescue medication was IRMS tablets. Primary measures of efficacy on the final day were time to first rescue medication and total dose of rescue as a % of total daily dose (TDD) of morphine (%IRMS). Secondary measures were: daily—visual analogue scale (VAS) of pain intensity, quality of sleep, and incidence of morphine-related side effects; final day—VAS and verbal rating scale (VRS) of pain intensity, VRS of pain control, and patient global assessment of pain control and investigator global assessment of efficacy. 152 patients completed final day assessments at 28 centres in the U.S.A.. Mean age was 61 yrs and TDD of morphine was 138 mg. 54 patients were treated with K q24h, 45 with K q12h, 53 with MSC. The number requiring rescue on the final day was K q24h 46%, K q12h 51%, MSC 55%. Time to first rescue was K q24h 6.8 h, K q12h 7.5 h, MSC 6.3 h. %IRMS was K q24h 39.2, K q12h 29.2, MSC 42.9. There were no significant differences for all measures. Patient global assessment (good or very good) significantly favoured K q24h over MSC (K q24h 89%, K q12h 76%, MSC 68%,  $P = 0.018$ ). There were no significant differences for other secondary measures. Kadian<sup>TM</sup>/Kapanol<sup>TM</sup> q24h and q12h had efficacy and safety similar to MSC q12h but had the added advantage of 12 to 24 hourly administration with a trend to less rescue medication use. Patient global assessment significantly favoured Kapanol<sup>TM</sup>/Kadian<sup>TM</sup>.

compare health related quality of life (QoL). Patients receiving oral morphine for cancer pain from 44 U.K. palliative care centres were randomised to receive 15 days FEN followed by 15 days MOR or vice versa; 202 patients entered the study and 110 completed it (mean age 61.5, 44.5% female). Immediate release oral morphine was available at any time for breakthrough pain. Cross-over comparisons were available from 127 patients. Pain levels were similar in both groups ( $P = 0.296$ ) but during the FEN phase patients experienced significantly less constipation ( $P < 0.001$ ) and nausea ( $P = 0.04$ ). The proportion of patients reporting 'quite a bit' or 'much' constipation was 34.8% in the MOR phase and 15.0% in the FEN phase, figures for nausea were 20.3% and 14.9% respectively; 60% (73/122) of patients preferred FEN ( $P = 0.037$ , binomial test), 14 (10%) did not distinguish between treatments. Further symptoms and scales from the EORTC QLQ-C30 QoL questionnaire and patient daily diary data on pain, sleep and sedation will be presented.

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### ORAL METHADONE FOR THE TREATMENT OF CANCER PAIN

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Methadone is an opioid analgesic drug still little used in cancer pain therapy. In a prospective study 162 advanced cancer patients with pain were treated with oral methadone. The aims of the study were: to assess the analgesic activity of methadone over time, the dosages of drug required for maintaining analgesia and side effects. Pain intensity before (TO) and during treatment (0–90 days) was evaluated by the Integrated Score (range 0–240), side effects (insomnia, drowsiness, confusion, xerostomia, nausea, vomiting, constipation and breathing difficulty) were evaluated through a Likert type scale with four points (no, a little, a lot, very much). Pain relief was calculated in respect to TO at 7–15–30–45–60–90 days. The results of the study show a significant mean reduction of pain of 25 points in the Score in respect to TO which was maintained all through the assessment period. The average of the mean daily dosages (calculated as mean doses at each evaluation time) used for pain control was 14 mg for 1st week of treatment and was gradually increased to 23 mg/day during the last week. Only a slight increase in drowsiness was observed. We believe that oral methadone should be considered as a valid alternative to oral morphine in cancer pain treatment due to its analgesic efficacy, tolerability and its low cost.

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### TTS-FENTANYL VS ORAL MORPHINE IN CANCER PAIN

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This was a multicentre, open, randomised, cross-over study of transdermal fentanyl (FEN) and sustained release oral morphine (MOR) to