



PATIENT SAFETY September 2004

1: Am J Med. 2004 Jul 15;117(2):100-6.

Risk of serious upper gastrointestinal and cardiovascular thromboembolic complications with meloxicam.

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PURPOSE: To assess the risk of serious gastrointestinal and thromboembolic complications with approved doses of meloxicam. **METHODS:** We pooled data from clinical trials of meloxicam at doses of 7.5 or 15 mg/d. A blinded gastrointestinal adjudication committee used prespecified criteria to identify gastric or duodenal perforation, gastric outlet obstruction, or hemodynamically important upper gastrointestinal bleeding. For analysis of thromboembolic complications, investigator-reported events were analyzed without adjudication. **RESULTS:** We analyzed data from 24,196 patients from 28 trials, most of whom had been followed for up to 60 days. Of these patients, 13,118 received meloxicam (10,158 received a daily dose of 7.5 mg and 2960 received 15 mg), 5283 were treated with diclofenac 100 mg, 181 received diclofenac 150 mg, 5371 were treated with piroxicam 20 mg, and 243 received naproxen 500 mg twice daily. Patients who received 7.5 mg of meloxicam daily had a 0.03% risk of serious upper gastrointestinal events, which was significantly lower than the risk in those who received diclofenac, naproxen, or piroxicam ($P < 0.02$). With the 15 mg daily dose of meloxicam, this risk was significantly different only when compared with piroxicam ($P = 0.03$). The risk of thromboembolic events in patients treated with meloxicam at either dose was lower than with diclofenac, but similar to that observed with piroxicam and naproxen. **CONCLUSION:** This pooled analysis of 24,196 patients demonstrates that meloxicam has a favorable gastrointestinal and thromboembolic safety profile. However, only a small number of patients were followed for more than 60 days, and meaningful comparisons were not possible in this subgroup.

Publication Types:

Clinical Trial

PMID: 15234645 [PubMed - indexed for MEDLINE]

2: Am J Ophthalmol. 2004 Jul;138(1):147-9.

Transpupillary thermotherapy for subfoveal neovascularization secondary to group 2A idiopathic juxtafoveolar telangiectasis.

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PURPOSE: To evaluate the efficacy and safety of transpupillary thermotherapy (TTT) for subfoveal neovascularization (SRNVM) in patients with group 2A Idiopathic Juxtafoveolar Telangiectasis (IJFT). **DESIGN:** Nonrandomized interventional case series. **METHODS:** We performed TTT for subfoveal SRNVM in 14 eyes of 13 patients with group 2A IJFT, who were referred to our tertiary care center. We evaluated visual outcome and SRNVM closure rate in these patients. **RESULTS:** After a mean follow-up period of 8.65 months, 92.3% of treated eyes had stabilization or improvement in visual acuity as well as regression of SRNVM by fluorescein angiography (FA). One SRNVM showed persistent leakage. One patient worsened by more than 2 Snellen lines; one required retreatment. **CONCLUSION:** Transpupillary thermotherapy may be a safe and useful alternative treatment option for patients with group 2A IJFT with subfoveal SRNVM. PMID: 15234300 [PubMed - indexed for MEDLINE]

3: Am J Ophthalmol. 2004 Jul;138(1):146-7.
Bilateral intraocular foreign bodies simulating crystalline lens.
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PURPOSE: To report a case of large bilateral intraocular foreign bodies mistaken for crystalline lens on computed tomography (CT). **DESIGN:** Case report. **METHODS:** A 24-year-old man was referred after bilateral open globe repair following a motor vehicle accident. Preoperatively, the CT scan had been read as "Right eye posteriorly dislocated lens. No evidence of foreign bodies." **RESULTS:** The patient underwent left eye cataract extraction with removal of a 7 x 5 x 5 mm piece of glass buried in the crystalline lens. The patient subsequently underwent right eye pars plana vitrectomy, removal of another piece of glass measuring 6 x 5 x 5 mm, retinal detachment surgery, and corneal grafting. **CONCLUSIONS:** Current safety standards require auto glass to fracture into pieces of a specific size to minimize laceration and missile injury. These pieces of glass may have a shape and size similar to the crystalline lens but have higher radiodensity on CT scan.
Publication Types:
Case Reports
PMID: 15234299 [PubMed - indexed for MEDLINE]

4: Am J Physiol Gastrointest Liver Physiol. 2004 Aug;287(2):G363-9.
Effect of oral CCK-1 agonist GI181771X on fasting and postprandial gastric functions in healthy volunteers.
Castillo EJ, Delgado-Aros S, Camilleri M, Burton D, Stephens D, O'Connor-Semmes R, Walker A, Shachoy-Clark A, Zinsmeister AR.
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CCK influences satiation and gastric and gallbladder emptying. GI181771X is a novel oral CCK-1 agonist; its effects on gastric emptying of solids, accommodation, and postprandial symptoms are unclear. Effects of four dose levels of the oral CCK-1 agonist GI181771X and placebo on gastric functions and postprandial symptoms were compared in 61 healthy men and women in a randomized, gender-stratified, double-blind, double-dummy placebo-controlled, parallel group study. Effects of 0.1, 0.5, and 1.5 mg of oral solution and a 5.0-mg tablet of

G1181771X on gastric emptying of solids by scintigraphy, gastric volume by (99m)Tc-single photon emission computed tomographic imaging, maximum tolerated volume of Ensure, and postprandial nausea, bloating, fullness, and pain were studied. On each of 3 study days, participants received their randomly assigned treatment. Adverse effects and safety were monitored. There were overall group effects of G1181771X on gastric emptying ($P < 0.01$) and fasting and postprandial volumes ($P = 0.036$ and 0.015 , respectively). The 1.5-mg oral solution of G1181771X significantly delayed gastric emptying of solids ($P < 0.01$) and increased fasting ($P = 0.035$) gastric volumes without altering postprandial ($P = 0.056$) gastric volumes or postprandial symptoms relative to placebo. The effect of the 5.0-mg tablet on gastric emptying of solids did not reach significance ($P = 0.052$). Pharmacokinetic profiles showed the highest area under the curve over 4 h for the 1.5-mg solution and a similar area under the curve for the 0.5-mg solution and 5-mg tablet. Adverse effects were predominantly gastrointestinal and occurred in a minority of participants. G1181771X delays gastric emptying of solids and exhibits an acceptable safety profile in healthy participants. CCK-1 receptors can be modulated to increase fasting gastric volume.

Publication Types:

Clinical Trial

Randomized Controlled Trial

PMID: 15246968 [PubMed - indexed for MEDLINE]

5: Am J Phys Med Rehabil. 2004 Aug;83(8):575-83.

Physiatry: medical errors, patient safety, patient injury, and quality of care.

DeLisa JA.

Department of Physical Medicine and Rehabilitation, UMDNJ-New Jersey Medical School, Newark, NJ, USA.

Publication Types:

Review

Review, Tutorial

PMID: 15277958 [PubMed - indexed for MEDLINE]

6: Ann Intern Med. 2004 Aug 17;141(4):326-7.

Comment on:

Ann Intern Med. 2004 Jan 6;140(1):33-6.

The patient safety movement will help, not harm, quality.

Wachter RM, Shojanian KG.

Publication Types:

Comment

Letter

PMID: 15313760 [PubMed - indexed for MEDLINE]

7: Arch Intern Med. 2004 Aug 9-23;164(15):1662-8.

Clinicians' perceptions of the problem of antimicrobial resistance in health care facilities.

Giblin TB, Sinkowitz-Cochran RL, Harris PL, Jacobs S, Liberatore K, Palfreyman MA, Harrison EI, Cardo DM; CDC Campaign to Prevent Antimicrobial Resistance Team.

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BACKGROUND: Many clinicians do not comply with guidelines regarding antimicrobial resistance (AR). In response, the Centers for Disease Control and Prevention developed a national Campaign to Prevent Antimicrobial Resistance in

Healthcare Settings that presents 4 strategies and 12 evidence-based steps. METHODS: To assess clinicians' perceptions of AR, barriers and facilitators to preventing AR, and how best to reach clinicians, a questionnaire and 4 focus groups were conducted after presentation of the Campaign at 4 Pittsburgh Regional Healthcare Initiative hospitals. RESULTS: One hundred seventeen clinicians completed the questionnaire; 28 participated in the focus groups. Clinicians were significantly more likely to perceive that AR was a problem nationally than in their own institution (95% vs 77%; $P < .001$) or practice (95% vs 65%; $P = .002$), consistent with focus group results (93% nationally vs 46% institution or practice). The 3 Campaign steps with the most barriers to implementation were "Treat infection, not colonization" (35%), "Stop treatment when infection is cured or unlikely" (35%), and "Practice antimicrobial control" (33%). Clinicians in the focus groups cited the additional barriers of the health care culture, lack of knowledge, and the nursing shortage; facilitators included education, information technology, and consults. Computer programs, posters, and local data were suggested for reaching clinicians about AR. CONCLUSIONS: Clinicians perceive AR to be a complex national problem but less relevant to their own institution or practice. Providing clinicians with information and steps for preventing AR, as in the Campaign, may affect their perceptions of the problem and motivate them to take actions to ensure patient safety.

Publication Types:

Multicenter Study

PMID: 15302636 [PubMed - indexed for MEDLINE]

8: Br J Cancer. 2004 Aug 2;91(3):441-6.

Interstitial photodynamic therapy as salvage treatment for recurrent head and neck cancer.

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Interstitial photodynamic therapy (IPDT) is a technique for applying photodynamic therapy (PDT) to internal tumours using light delivered via fibres inserted percutaneously. This phase I-II study assessed the safety and efficacy of IPDT for patients with persistent or recurrent head and neck cancer unsuitable for further treatment with surgery, radiotherapy or chemotherapy, recruited for 'last hope' salvage treatment. Patients were sensitised with 0.15 mg kg⁻¹ mTHPC (meso-tetrahydroxyphenyl chlorin) 4 days prior to light delivery from fibres inserted directly into the target tumour (20 J per site at 652 nm) under image guidance. In all, 45 patients were treated. Nine achieved a complete response. Five are alive and free of disease 10-60 months later. Symptomatic relief (mainly for bleeding, pain or tumour debulking) was achieved in a further 24. The median survival (Kaplan-Meier) was 16 months for the 33 responders, but only 2 months for the 12 nonresponders. The only serious complication was a carotid blow out 2 weeks after PDT. No loss of function was detected in nerves encased by treated tumours. Interstitial photodynamic therapy provides worthwhile palliation with few complications and occasional long-term survivors for otherwise untreatable advanced head and neck cancers. It is a treatment option worth adding to those available to integrated head and neck oncology teams.

Publication Types:

Clinical Trial

Clinical Trial, Phase I

Clinical Trial, Phase II

PMID: 15238981 [PubMed - indexed for MEDLINE]

9: Br J Cancer. 2004 Aug 2;91(3):453-8.

Phase II study of weekly oxaliplatin and 24-h infusion of high-dose 5-fluorouracil and folinic acid in the treatment of advanced gastric cancer.

Chao Y, Yeh KH, Chang CJ, Chen LT, Chao TY, Wu MF, Chang CS, Chang JY, Chung CY,

Kao WY, Hsieh RK, Cheng AL.

Taipei Veterans General Hospital, Taipei, Taiwan.

To investigate the efficacy and safety of combining weekly oxaliplatin with weekly 24-h infusion of high-dose 5-fluorouracil (5-FU) and folinic acid (FA) in treatment of patients with advanced gastric cancer. Patients with histologically confirmed, locally advanced or recurrent/metastatic gastric cancer were studied. Oxaliplatin 65 mg m(-2) 2-h intravenous infusion, and 5-FU 2600 mg m(-2) plus FA 300 mg m(-2) 24-h intravenous infusion, were given on days 1 and 8, repeated every 3 weeks. Between January 2001 through January 2002, 55 patients were enrolled. The median age was 64 years (range: 22-75). In all, 52 patients (94.5%) had recurrent or metastatic disease and three patients had locally advanced disease. Among 50 patients evaluable for tumour response, 28 patients achieved partial response, with an overall response rate of 56% (95% confidence interval (CI): 41.8-70.3%). All 55 patients were evaluated for survival and toxicities. Median time to progression and overall survival were 5.2 and 10.0 months, respectively, during median follow-up time of 24.0 months. Major grades 3-4 toxicities were neutropenia in 23 cycles (7.1%) and thrombocytopenia in 16 cycles (5.0%). Treatment was discontinued for treatment-related toxicities in nine patients (16.4%), of whom eight were due to oxaliplatin-related neurotoxicity. One patient (1.8%) died of neutropenic sepsis. This oxaliplatin-containing regimen is effective in the treatment of advanced gastric cancer. Except for neurotoxicity that often develops after prolonged use of oxaliplatin, the regimen is well tolerated.

Publication Types:

Clinical Trial

Clinical Trial, Phase II

Multicenter Study

PMID: 15226770 [PubMed - indexed for MEDLINE]

10: Eur Neuropsychopharmacol. 2004 Aug;14(4):301-6.

Zolpidem is not superior to temazepam with respect to rebound insomnia: acontrolled study.

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This randomised controlled trial was conducted to compare zolpidem to an equivalent dose of temazepam with respect to subjective rebound insomnia after cessation of 4 weeks of treatment in chronic insomnia (zolpidem 10 mg, n=79; temazepam 20 mg, n=84). Both agents improved total sleep time (TST) as well as sleep onset latency (SOL) significantly during the 4 treatment weeks. Prevalence rates for rebound insomnia, defined as a worsening of TST or SOL of more than 40% compared to baseline, were 27% for TST and 53% for SOL in the Zolpidem condition and 26% and 58%, respectively, in the temazepam condition. No significant differences were found between both agents with respect to rebound insomnia, nor with respect to their efficacy or safety. We conclude that in clinical practice zolpidem has no advantages over temazepam with respect to rebound insomnia.

Publication Types:
Clinical Trial
Randomized Controlled Trial

11: Hosp Peer Rev. 2004 Jul;29(7):89-93.
Avoid disasters during your next JCAHO survey: quality managers share secrets.
[No authors listed]
PMID: 15244092 [PubMed - indexed for MEDLINE]

12: Hosp Peer Rev. 2004 Jul;29(7):suppl 1-2.
Patient Safety Alert. Finding root causes without blame helps eliminate errors.
[No authors listed]
PMID: 15244091 [PubMed - indexed for MEDLINE]

13: J Adv Nurs. 2004 Aug;47(3):329-39.
Using a Nursing Minimum Data Set with older patients with dementia in an acute care setting.
Park M, Delaney C, Maas M, Reed D.
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BACKGROUND: Many older people with dementia are admitted to acute care settings suffering from comorbidities. These and their treatments can lead to confusion in these patients, adding to their existing cognitive deficits, and this may not be recognized by care staff. The care of such patients is complex and requires multidisciplinary team input. The purposes of the Nursing Minimum Data Set are to describe the nursing care of patients in a variety of settings and to establish comparability of nursing data across clinical populations, settings and time. **AIMS:** This paper reports a study to describe the characteristics of hospitalized older patients with dementia and nursing diagnoses and nursing interventions for these patients, and to identify trends in the nursing care provided over a 3-year period using a Nursing Minimum Data Set from a community hospital in the United States of America. **METHODS:** Secondary data analysis was conducted in 2000 on a large clinical discharge data set containing Nursing Minimum Data Set elements. The sample included 597 elders with dementia among a total of 7772 older patients who were discharged between 1996 and 1998. **RESULTS:** The most common comorbidity was hypertension (n = 123, 21%), followed by cardiac dysrhythmias (n = 80, 13%). The most frequent nursing diagnoses were altered health maintenance (n = 419, 84%), knowledge deficit (n = 357, 71%), potential for injury (n = 242, 48%), potential for infection (n = 230, 46%), pain (n = 184, 37%), impaired physical mobility (n = 169, 34%), and altered thought process (n = 144, 29%). The most frequent interventions were discharge planning (n = 340, 68%), surveillance safety (n = 195, 39%), fall prevention (n = 175, 35%), teaching: disease process (n = 166, 33%), learning facilitation (n = 148, 30%), and infection protection (n = 147, 29%). **CONCLUSIONS:** The results provide a description of nursing diagnoses and interventions for elders with dementia in an acute care setting using the Nursing Minimum Data Set framework. They identify the need to develop staff education programmes for individualized care of older patients with dementia. In addition, they support the need for continued work on linkage of the nursing care elements of the Nursing Minimum Data Set, including nursing diagnoses, nursing interventions, and

nursing-sensitive outcomes.
PMID: 15238128 [PubMed - indexed for MEDLINE]

14: J Adv Nurs. 2004 Aug;47(3):251-9.

Patient safety and comfort during transfers in relation to nurses' work technique.

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BACKGROUND: The work technique used by health care professionals in patient transfer tasks affects the musculoskeletal load on the professionals, but probably also the safety and well-being of patients being transferred; it is thus a matter of quality of care. **AIMS:** The aim of this paper is to report a study exploring the relations between the work technique of nurses in patient transfer tasks, and patients' perceptions of safety and comfort during the transfers. **METHODS:** The work technique used by 102 nurses at orthopaedic wards to perform two common patient transfers: one transfer higher up in bed and one from bed to wheelchair, were examined using video recordings and an observation instrument. A work technique score for each performed transfer was calculated, indicating the level of musculoskeletal safety for the nurse. Nurses assessed their own work technique and patients rated the perceived safety and comfort on bipolar scales directly after each transfer. **RESULTS:** Patients' perceptions of safety and comfort were positively correlated to the work technique score in both transfers. Patients felt safer and more comfortable during transfers performed with a safe technique, according to the work technique score, than during those performed with a poor technique. Patients' ratings of safety in the transfer from bed to wheelchair, and their ratings of comfort in both transfers, were positively correlated to nurses' assessments of their own work technique. However, the correlation coefficients were rather low. **CONCLUSIONS:** The results support the existence of a relationship between nurses' skills in patient transfers and quality of patient care.

Publication Types:

Multicenter Study

PMID: 15238119 [PubMed - indexed for MEDLINE]

15: J Adv Nurs. 2004 Aug;47(3):251-9.

Patient safety and comfort during transfers in relation to nurses' work technique.

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BACKGROUND: The work technique used by health care professionals in patient transfer tasks affects the musculoskeletal load on the professionals, but probably also the safety and well-being of patients being transferred; it is thus a matter of quality of care. **AIMS:** The aim of this paper is to report a study exploring the relations between the work technique of nurses in patient transfer tasks, and patients' perceptions of safety and comfort during the transfers. **METHODS:** The work technique used by 102 nurses at orthopaedic wards to perform two common patient transfers: one transfer higher up in bed and one from bed to wheelchair, were examined using video recordings and an observation instrument. A work technique score for each performed transfer was calculated, indicating the level of musculoskeletal safety for the nurse. Nurses assessed their own work technique and patients rated the perceived safety and comfort on bipolar scales directly after each transfer. **RESULTS:** Patients' perceptions of safety and comfort were positively correlated to the work technique score in

both transfers. Patients felt safer and more comfortable during transfers performed with a safe technique, according to the work technique score, than during those performed with a poor technique. Patients' ratings of safety in the transfer from bed to wheelchair, and their ratings of comfort in both transfers, were positively correlated to nurses' assessments of their own work technique. However, the correlation coefficients were rather low. CONCLUSIONS: The results support the existence of a relationship between nurses' skills in patient transfers and quality of patient care.

Publication Types:

Multicenter Study

PMID: 15238119 [PubMed - indexed for MEDLINE]

16: J Adv Nurs. 2004 Jul;47(2):223-9.

Characteristics of falls in hospitalized patients.

Kerzman H, Chetrit A, Brin L, Toren O.

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BACKGROUND: The high incidence of patient falls in a hospital setting is a major concern in any health system. Research findings have reported the risk factors for these falls as age, gender, certain medications, mental status, chronic diseases and environmental factors. Falls may lead to fear, pain, slight or severe injuries, increase the duration of hospital stay, cause patient discomfort and affect quality of life. AIM: The aim of this paper is to report a study of the characteristics of patient falls during hospitalization in 1998 and compare them with those in the period 1978-1981. METHODS: A retrospective study was performed in a large, 2000-bed medical center in Israel. Reports of 711 fall incidents in 1998 were compared with 328 reports in 1978-1981. Information gathered included age, gender, department, shift, reasons, severity of injury, tests and treatment after injury. RESULTS: The rates of falls per 1000 admissions in psychiatric, elder care and rehabilitation departments in 1998 were statistically significantly higher than in the earlier period. Rates of 115, 91, 85, respectively, per 1000 admissions were reported in 1998 compared with 34, 9, 19, respectively, in the period 1978-1981. The percentage of reported falls in the younger age group (under 50) was higher in the later survey (1998), and a higher proportion occurred outside the patient's room. Most of the reported falls in 1998 occurred during the morning shift ($P < 0.001$). CONCLUSIONS: The increased number of falls could be an outcome of increased awareness. Nevertheless, the causes and place of falls differ for the two periods. Some of the reasons may be related to an intervention programme carried out after the first survey. The latest survey results will serve as an important basis for a further intervention programme in specific departments to ensure patient safety.

PMID: 15196196 [PubMed - indexed for MEDLINE]

17: J Clin Nurs. 2004 Jul;13(5):547-54.

Blood exposure: factors promoting health care workers' compliance with guidelines in connection with risk.

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BACKGROUND: Health care workers compliance with guidelines, universal precautions, in connection with tasks that could involve contact with patient's blood is unsatisfactory. In a previous paper, we identified different forces

that undermine compliance. Socialization into infection control, routinization, stereotyping, perceptions of patients' wishes and the presence of competing values and norms are examples of such forces. AIMS AND OBJECTIVES: The aim of this article is to describe and analyse different forces that promote adherence to universal precautions. Behavioural variations are seen as a consequence of differences between wards with regard to the safety culture. Safety culture is conceptualized as the outcome of a constant interplay between deactivating and reactivating forces. In this article the focus is on the latter. METHOD: The grounded theory approach. Data were collected through interviews with nurses and assistant nurses. RESULTS: The charge nurse, informal leaders, students, infection control nurses, type of work, availability of equipment, blood-exposure incidents and media-coverage of infectious diseases are described as potentially important for compliance. The properties these agents must possess in order to be influential are also described. RELEVANCE TO CLINICAL PRACTICE: The outcome of an occupationally acquired infection can be fatal. Hence it is important that health care workers take protective measures. The results imply that mere information about safe practices alone is insufficient to achieve that goal. All factors of importance for compliance must be taken in to consideration in clinical work and in education.
PMID: 15189407 [PubMed - indexed for MEDLINE]

18: J Clin Oncol. 2004 Aug 15;22(16):3269-76. Epub 2004 Jul 12.

Comment in:

J Clin Oncol. 2004 Aug 15;22(16):3212-4.

Phase I study of an immunomodulatory thalidomide analog, CC-4047, in relapsed or refractory multiple myeloma.

Schey SA, Fields P, Bartlett JB, Clarke IA, Ashan G, Knight RD, Streetly M, Dalgleish AG.

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PURPOSE: To assess the safety, efficacy, and immunomodulatory effects of CC-4047 (Actimid; Celgene, San Diego, CA) in patients with relapsed or refractory myeloma. PATIENTS AND METHODS: Twenty-four relapsed or refractory patients were treated with a dose-escalating regimen of oral CC-4047. Clinical responses and adverse effects were identified, and peripheral T-cell subsets, serum cytokines, and proangiogenic factors were evaluated. RESULTS: CC-4047 was tolerated with no serious nonhematologic adverse events. All patients were eligible for analysis. Toxicity criteria during the initial 4 weeks of study were used to define the maximum-tolerated dose (MTD). During this period, one patient withdrew with a deep vein thrombosis (DVT) probably caused by an undiagnosed primary melanoma with lymphadenopathy in the groin, one patient withdrew because of progressive disease (PD), and three patients discontinued with neutropenia. Nineteen of 24 patients continued on treatment beyond 4 weeks to PD or development of a serious adverse event. Three further patients developed a DVT at 4, 9, and 11 months. Treatment resulted in a greater than 25% reduction in paraprotein in 67% of patients, 13 patients (54%) experienced a greater than 50% reduction in paraprotein, and four (17%) of 24 patients entered complete remission. The MTD was 2 mg/d. All patients showed increased CD45RO expression on CD4(+) and CD8(+) cells, with a concomitant decrease in CD45RA(+) cells. CC-4047 treatment was associated with significantly increased serum interleukin (IL)-2 receptor and IL-12 levels, which is consistent with activation of T cells and monocytes and

macrophages. CONCLUSION: This study demonstrates the safety and efficacy of CC-4047. The MTD of CC-4047 orally was 2 mg/d. This is the first report demonstrating in vivo T-cell costimulation by this class of compound, supporting a potential role for CC-4047 as an immunostimulatory adjuvant treatment.

Publication Types:

Clinical Trial

Clinical Trial, Phase I

PMID: 15249589 [PubMed - indexed for MEDLINE]

19: J Clin Oncol. 2004 Aug 1;22(15):3003-15. Epub 2004 Jun 21.

Comment in:

J Clin Oncol. 2004 Aug 1;22(15):2975-7.

Safety, pharmacokinetics, and activity of ABX-EGF, a fully human anti-epidermal growth factor receptor monoclonal antibody in patients with metastatic renal cell cancer.

Rowinsky EK, Schwartz GH, Gollob JA, Thompson JA, Vogelzang NJ, Figlin R, Bukowski R, Haas N, Lockbaum P, Li YP, Arends R, Foon KA, Schwab G, Dutcher J. Institute for Drug Development, Cancer Therapy and Research Center, 7979 Wurzbach Rd, 4th Floor, Zeller Building, San Antonio, TX 78229, USA. erowinsk@idd.org

PURPOSE: To determine the antitumor activity of ABX-EGF, a fully human monoclonal antibody to the epidermal growth factor receptor (EGFr), in previously treated patients with metastatic renal cell carcinoma, and to characterize its toxicity, immunogenicity, pharmacokinetics, and pharmacodynamics. PATIENTS AND METHODS: The antitumor activity, as well as the toxicity, pharmacokinetics, pharmacodynamics, and immunogenicity of ABX-EGF, were assessed. RESULTS: Eighty-eight patients were treated with ABX-EGF doses of 1.0, 1.5, 2.0, or 2.5 mg/kg weekly with no loading dose. EGFr immunostaining was performed on 76 tumor biopsy specimens (86%), and 69 (91%) scored positive. Major responses occurred in three patients, and two patients had minor responses. Forty-four patients (50%) also had stable disease at their first 8-week assessment, and the median progression-free survival (PFS) was 100 days (95% CI, 58 to 140 days). Low hemoglobin and high alkaline phosphatase predicted for short PFS. The principal toxicity, an acneiform rash, occurred in 68%, 95%, 87%, and 100% of patients who received at least three doses of ABX-EGF at 1.0, 1.5, 2.0, and 2.5 mg/kg/wk, respectively. A trend indicated that the severity of the rash may relate to PFS. No human antihuman antibodies were detected. ABX-EGF

pharmacokinetics fit a model that incorporated both linear and saturable EGFr-mediated clearance mechanisms, and interindividual variability was low. At 2.5 mg/kg/wk, ABX-EGF concentrations throughout treatment exceeded those estimated to saturate nonlinear clearance and inhibit xenograft growth by 90%. CONCLUSION: ABX-EGF was generally well tolerated. The objective response rate was low in previously treated patients with metastatic renal cell carcinoma. Although skin rash may be a pharmacodynamic marker of drug action, its potential as a surrogate marker of clinical benefit requires further evaluation.

Publication Types:

Multicenter Study

PMID: 15210739 [PubMed - indexed for MEDLINE]

20: J Clin Oncol. 2004 Jul 1;22(13):2662-70.

Liposome-encapsulated doxorubicin in combination with standard agents

(cyclophosphamide, vincristine, prednisone) in patients with newly diagnosed AIDS-related non-Hodgkin's lymphoma: results of therapy and correlates of response.

Levine AM, Tulpule A, Espina B, Sherrod A, Boswell WD, Lieberman RD, Nathwani BN, Welles L.

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PURPOSE: To evaluate the safety and efficacy of liposomal doxorubicin (Myocet; Medeus Pharma Ltd, Herts, UK) when substituted for doxorubicin in the CHOP regimen (cyclophosphamide, doxorubicin, vincristine, prednisone) in patients with newly diagnosed AIDS-related non-Hodgkin's lymphoma (AIDS-NHL).

Secondary

objectives were to assess the impact of HIV viral control on response and survival, and to correlate MDR-1 expression with outcome. **PATIENTS AND METHODS:**

Liposomal doxorubicin at doses of 40, 50, 60, and 80 mg/m² was given with fixed doses of cyclophosphamide, vincristine, and prednisone every 21 days. All patients received concurrent highly active antiretroviral therapy. NHL tissues were evaluated for multidrug resistance (MDR-1) expression. **RESULTS:** Twenty-four patients were accrued. 67% had high or high-intermediate International Prognostic Index scores; the median CD4 lymphocyte count was 112/mm³ (range, 19/mm³ to 791/mm³). No dose-limiting toxicities were observed at any level, with myelosuppression being the most frequent toxicity. Overall response rate was 88%, with 75% complete responses (CRs), and 13% partial responses. The median duration of CR was 15.6+ months (range, 1.7 to 43.5+ months). Effective HIV viral control during chemotherapy was associated with significantly improved survival (P = .027), but CRs were attained independent of HIV viral control.

MDR-1 expression did not correlate with response, suggesting that the liposomal doxorubicin may evade this resistance mechanism. **CONCLUSION:** Liposomal doxorubicin in combination with cyclophosphamide, vincristine, and prednisone is active in AIDS-NHL, with complete remissions achieved in 75% independent of HIV viral control or tissue MDR-1 expression. HIV viral control is associated with a significant improvement in survival. Additional studies are warranted.

Publication Types:

Clinical Trial

Clinical Trial, Phase I

Clinical Trial, Phase II

PMID: 15226333 [PubMed - indexed for MEDLINE]

21: J Pain Symptom Manage. 2004 Jul;28(1):72-95.

A comprehensive review of clinical trials on the efficacy and safety of drugs for the treatment of low back pain.

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A systematic review involving 50 randomized controlled trials (4,863 patients) published since 1980 was undertaken with the objective of assessing efficacy and safety of low back pain (LBP) medications. The methodological quality of each trial was evaluated based on a standardized system. Quality scores ranged from 26 to 82 points on a 100-point scale (from 0 to 100), indicating an overall moderate quality of the trials reviewed. Limited evidence was found regarding the effectiveness of drug treatments for LBP and current studies focused on short-term usage of the therapies. Available evidence supported the effectiveness of non-selective nonsteroidal anti-inflammatory drugs (NSAIDs) in

acute and chronic LBP, of muscle relaxants in acute LBP, and of antidepressants in chronic LBP; safety results were heterogeneous. More rigorously designed trials should be implemented to establish comparative efficacy and safety of drugs used to treat chronic and acute LBP.

Publication Types:

Review

Review Literature

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22: J Pain Symptom Manage. 2004 Jul;28(1):59-71.

Efficacy and safety of extended-release, once-daily tramadol in chronic pain: a randomized 12-week clinical trial in osteoarthritis of the knee.

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The efficacy and safety of a once-daily extended-release formulation of tramadol hydrochloride (tramadol ER) was evaluated in patients with moderate to severe chronic pain of osteoarthritis (OA). This was a randomized, double-blind, placebo-controlled, parallel-group, 12-week study. Eligible patients with radiographically confirmed OA of the knee meeting the American College of Rheumatology diagnostic criteria, defined by knee pain and presence of osteophytes, plus at least age >50 years, morning stiffness <30 minutes in duration, and/or crepitus, entered a 2-7 day washout period during which all analgesics were discontinued. When pain at the index knee joint reached > or =40 mm (0-100 mm VAS), patients were randomized to tramadol ER or placebo.

Tramadol

ER was initiated at 100 mg QD and increased to 200 mg QD by the end of 1 week of treatment. After the first week, further increases to tramadol ER 300 mg or 400 mg QD were allowed. Outcome measures included Arthritis Pain Intensity Visual Analogue Scale (VAS), Western Ontario and McMaster Universities Arthritis Scale (WOMAC) Pain, Stiffness, Physical Function VAS subscales, Patient and Physician Global Assessment of Therapy, Sleep, dropouts due to insufficient therapeutic effect, and adverse events. Two hundred forty-six patients were randomized (tramadol ER 124, placebo 122). There were no baseline differences between the two treatments. The mean age was 61 years, mean duration of OA 12.9 years, and the mean tramadol ER dose was 276 mg QD. All efficacy outcome measures favored tramadol ER over placebo. On the primary outcome variable of average change from baseline in Arthritis Pain Intensity VAS over 12 weeks, tramadol ER was superior to placebo (least squares mean change from baseline: 30.4 mm vs. 17.7 mm, $P < 0.001$). Significant differences from placebo were evident at week 1, the first post-treatment visit. Similarly, outcomes on the WOMAC Pain, Stiffness and Physical Function subscales, the WOMAC Composite Scale, dropouts due to insufficient therapeutic effect, Patient and Physician Global Assessment of Therapy, and Sleep were all significantly better with tramadol ER than placebo ($P < 0.001$ to < 0.05). Treatment with tramadol ER results in statistically significant and clinically important and sustained improvements in pain, stiffness, physical function, global status, and sleep in patients with chronic pain. A once-a-day formulation of tramadol has the potential to provide patients increased control over the management of their pain, fewer interruptions in sleep and improved compliance.

Publication Types:

Clinical Trial

Randomized Controlled Trial

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