Musculoskeletal

MS1

PARENTERAL PARECOXIB FOLLOWED BY ORAL VALDECOXIB AFTER MAJOR GENERAL SURGERY REDUCES OPIOID CONSUMPTION AND OPIOID-RELATED SYMPTOMS

Katz JA[1], Ferrante FM[2], Neumann J[3], Rowinski W[4], Trzebicki J[4], Kosieradzki M[4], Brown MT[5], Boye M[5]
[1]Northwestern University Medical Center, Chicago, IL, USA; [2]UCLA, Los Angeles, CA, USA; [3]Charles University Teaching Hospital of 2nd Medical School, Prague 5, Prague, Czech Republic; [4]Medical University of Warsaw, Warsaw, Warsaw, Poland; [5]Pfizer Inc, New York, NY, USA

OBJECTIVES: To evaluate the clinical benefit of reduced opioid consumption using multimodal analgesia with intravenous (IV) and oral cyclooxygenase-2 (COX-2) specific inhibitors in combination with conventional analgesia vs conventional analgesia alone, in patients undergoing major general surgery. **METHODS:** In this double-blind, placebo-controlled trial, patients were randomized to parecoxib/valdecoxib (n = 533) parecoxib 40 mg IV on Day-one (day of surgery) then 20 mg IV/IM [intramuscular] q12h for three-days, then oral valdecoxib 20 mg q12h) for seven-days or placebo (n = 529). Supplemental analgesia was patient-controlled morphine during IV/IM dosing, and codeine/acetaminophen or hydrocodone/acetaminophen during oral dosing. Beginning Day-two, the patient-reported Opioid-Related Symptom Distress Scale (OR-SDS)—an original, validated instrument—was administered nightly at bedtime to assess ten opioid-related adverse effects. Patient distress attributed to each opioid-related adverse effect was assessed using verbal rating scales for frequency, severity, and bother, with clinically meaningful adverse effects (CMEs) defined as those rated as having occurred at least "frequently" or with at least "severe" intensity or resulting in at least a "somewhat bothered" level of distress. **RESULTS:** Opioid consumption was reduced by 37% ($P < 0.001$), 28% ($P < 0.004$), and 38% ($P < 0.002$) with parecoxib/valdecoxib vs. placebo on days two to four, respectively. Randomization to parecoxib/valdecoxib resulted in significantly reduced risk of clinically meaningful drowsiness (nominal $P < 0.001$) and fatigue (nominal $P < 0.001$). Across the ten OR-SDS adverse effects, 73% (378/520), 58% (291/502), and 46% (226/496) of patients randomized to placebo reported at least one CME on days two to four, respectively, compared with corresponding rates of 59% (307/520), 42% (215/512), and 28% (142/499) in the parecoxib/valdecoxib treatment group ($P < 0.001$). **CONCLUSION:** Compared with standard analgesia alone, treatment with parecoxib/valdecoxib plus standard analgesia after major general surgery significantly reduced opioid consumption and patient days with opioid-related CMEs. Newly developed OR-SDS is a useful validated instrument in documenting these findings.

MS2

CARDIOVASCULAR RISK FACTORS AT BASELINE IN USERS OF COXIBS COMPARED TO USERS OF NSAIDS

De Jong RB, Breekveldt-Postma NS, Goettsch WG, Herings RM
PHARMO Institute, Utrecht, Utrecht, Netherlands

OBJECTIVE: To assess the cardiovascular risk factors at baseline in Dutch patients prescribed cyclooxygenase-2 inhibitors (coxibs) compared to nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). **METHODS:** Data were obtained from the PHARMO database, which includes linked drug-dispensing records and hospital records of more than one million subjects in defined areas in the Netherlands. All users of celecoxib, rofecoxib or NSAIDs in the period January, 2001—December, 2003 were included in this retrospective population based cohort study. The presence of cardiovascular risk factors based on hospital admissions and drug use was compared in the year before the first prescription between users of coxibs or NSAIDs using logistic regression analyses. **RESULTS:** The cohort consisted of approximately 4,000 users of celecoxib, 34,000 users of rofecoxib and 326,000 users of NSAIDs. Users of coxibs more often were female (68% vs. 56%) and of higher age (average of 56 years vs. 45 years) compared to users of NSAIDs. Multivariate analyses including gender, age and prescriber showed that patients using celecoxib 1.3 times (95%CI: 1.05–1.59) more often had a history of hospital admissions for cardiovascular diseases compared to patients using NSAIDs. This association was not significant for users of rofecoxib. Other factors positively associated with the use of coxibs were previous hospitalizations for RA, OA and other diagnoses and previous use of gastroprotective agents. **CONCLUSIONS:** In general, users of coxibs seem to be less healthy then users of NSAIDs with higher cardiovascular risk factors at baseline. This difference should be taken into account when investigating the possible association between cardiovascular adverse events and use of coxibs.

MS3

ECONOMIC EVALUATION OF CONTROLLED-RELEASE OXYCODONE (OXYCONTIN® TABLETS) (CRO) VERSUS OXYCODONE/ACETAMINOPHEN (PERCOCET®) (OXY/APAP) FOR OSTEOARTHRITIS PAIN OF THE HIP OR KNEE

Marshall DA[1], Strauss ME[2], Pericak D[1], Buitendyk M[1], Codding C[3], Kim S[2], Torrance G[1]
[1]Innovus Research Inc, Burlington, ON, Canada; [2]Purdue Pharma L.P, Stamford, CT, USA; [3]Oklahoma Sports, Oklahoma City, OK, USA

OBJECTIVES: CRO is efficacious for persistent moderate to severe osteoarthritis pain based on well-controlled trials. Additionally, decision-makers require evidence of effectiveness in routine practice, and cost-effectiveness compared to standard therapy. **METHODS:** Open-label, active-controlled, randomized, naturalistic four-month study of analgesic effectiveness and cost-effectiveness of CRO vs. oxy/APAP. Outcomes and resource use were collected by telephone. Effectiveness was measured in 485 patients as the proportion having at least 20% improvement from baseline in Western Ontario and McMaster Universities Osteoarthritis Index pain score. Quality-adjusted-life-years (QALYs) were calculated from Health Utilities Index-3 scores. Cost-effectiveness was measured as cost/patient improved and QALYs gained from societal and health care perspectives using generic oxy/APAP (base case). Uncertainty was evaluated using multiple one-way sensitivity analyses and cost-effectiveness acceptability curves. **RESULTS:** In total, 62.2% vs. 45.9% ($p = 0.0003$) of patients improved with CRO and oxy/APAP respectively. Mean QALYs gained over four months with CRO compared to oxy/APAP was 0.0105 ($p = 0.1673$). Mean societal cost/patient over four months was US$6792 vs. US$6929 ($p = 0.3345$) for CRO and oxy/APAP, respectively. CRO was both more effective and less costly than oxy/APAP using the societal perspective (includes costs associated with time loss). Using a health care perspective (excludes costs associated with time loss), cost-effectiveness of CRO was US$4,500/patient improved and US$69,856/QALY gained. **CONCLUSIONS:** From the societal perspective, CRO was both more effective and less costly than oxy/APAP. From the health care perspective, CRO compared to generic oxy/APAP fell within the acceptable range of cost-effectiveness if decision-makers were willing-to-pay between US$50,000/QALY and US$100,000/QALY. These findings should be considered in decisions about treating osteoarthritis pain.