

# POSTER ABSTRACTS

## Analgesia

**1. Title:** Sex specific, estrogen-dependent modulation of spinal nociception via selective activation of kappa-opioid receptors in the rat

**Presenter:** Kera P. Lawson

**Biography:** Ms. Lawson is a doctoral candidate in the Department of Neurobiology and Neurotoxicology at Meharry Medical College. Her work focuses on sex differences in the modulation of pain.

**Abstract:**

**Background:** Partial kappa opioid receptor (KOR) agonists have been shown to produce sex-specific analgesic effects in clinical studies. However, relative contribution of KOR in those studies is uncertain since the partial kappa opioids used also show affinity to mu opioid receptors. Further, sex-related differences in the actions of kappa opioids in the spinal cord remain controversial.

**Objective:** To examine whether selective activation of KOR produces sex-specific modulation of spinal nociception in the rat and whether estrogen contributes to these differences.

**Methods:** Thermal nociceptive tail flick test was used to examine sex-specific modulation of spinal nociception in male, ovariectomized (OVX), estradiol-treated OVX, proestrous, and diestrous rats. Animals were surgically prepared under ketamine and xylazine anesthesia. Cannulae were implanted in the intrathecal space of the lumbosacral spinal cord. Tail flick testing was conducted 5 to 7 days after surgery. Estradiol benzoate (1 ng-100 µg/100 µl sesame oil) was administered subcutaneously in separate groups of OVX rats 48 h before testing. U50, 488H (25, 50, and 100 nmol/5 µl), a selective KOR agonist, was injected intrathecally in the lumbar spinal cord through the implanted cannula. Nor-binaltorphimine (nor-BNI, 87 nmol/5 ml, i.t.), a selective KOR antagonist, was administered 5 min prior to U50, 488H injection. Tail flick latencies (TFLs) were recorded at 10 min intervals for 120 min.

**Results:** Pre-drug baseline tail flick latencies were comparable in all groups. Intrathecal administration of U50, 488H produced significant increase in TFLs in proestrous and OVX female rats treated with estradiol, but failed to produce an effect in male, OVX and diestrous groups. Antinociceptive effects of U50, 488H were dose dependent in proestrous and OVX +E animals and were blocked by nor-BNI. Further, estrogen dose-dependently enhanced the effect of U50, 488H in OVX rats.

**Conclusions:** Selective activation of KOR produces estrogen-dependent, sex-specific modulation of spinal nociception in the rat.

**2. Title:** Integrated assessment of pain and rescue use in a nalbuphine ER trial

**Presenter:** David Verbel, MPH

**Biography:** Mr. Verbel has more than 10 years of industry and research experience focused on clinical trial design and predictive modeling. He is currently employed by Penwest Pharmaceuticals.

**Co-presenters:** Peter Lacouture, MS, PhD, Executive Director of Scientific/Medical Affairs, Magidom Discovery, LLC, Drug Discovery to Development; Tom Sciascia, MD, Chief Medical Officer, Senior Vice President, and Corporate Officer at Penwest Pharmaceuticals; Jacque Kuritzky, Director of Clinical Studies for

Penwest Pharmaceuticals; Evelyn Juma, CCRA, Manager of Clinical Trials for Penwest Pharmaceuticals; Brian Vogler, MS, Clinical Programmer and Data Specialist for Penwest Pharmaceuticals; Nathaniel Katz, MD, MS, President of Analgesic Research, Vice President for Medical Affairs and Director of Pain Research for Inflexion, Inc., Adjunct Assistant Professor of Anesthesia at Tufts University School of Medicine, and Director of the Program in Opioid Risk Management at Tufts Health Care Institute

**Abstract:**

**Background:** Defining efficacy in clinical trials of analgesic development has traditionally utilized patient reports of pain intensity. In placebo-controlled trials, drop-outs due to lack of efficacy (LOE) are expected; to reduce this drop-out rate, rescue medication is often provided. Proving a significant effect on pain can then be difficult, since efficacy is now influenced by the study medication and rescue medication. An integrated outcome variable, combining pain intensity and rescue use, may be more appropriate to accurately assess the efficacy of an analgesic. Nalbuphine is an established agonist-antagonist opioid analgesic being developed as an oral extended-release (ER) product.

**Objective:** To explore the utility of an integrated assessment of changes in pain intensity and rescue use to assess the analgesic activity of nalbuphine ER.

**Methods:** An IRB-approved, randomized, double-blind, placebo-controlled trial of oral nalbuphine ER in patients with osteoarthritis (OA) pain was conducted. 141 patients with OA, who met standard entrance criteria, were randomized to placebo or nalbuphine ER twice-daily and via a forced-titration design had their dose increased weekly up from 60 mg to 120 mg to 180 mg. Separate statistical analyses of pain intensity and rescue use were performed. In addition, an integrated outcome variable combining pain and rescue use described by Silverman et al was analyzed.

**Results:** No treatment differences were observed for pain intensity ( $p=0.275$ ) or rescue use ( $p=0.418$ ) alone; however a statistically significant nalbuphine ER treatment effect was observed for the integrated outcome variable ( $p=0.009$ ).

**Conclusions:** The utility of an integrated outcome variable combining both pain and rescue use was demonstrated in a prospective study. Additional exploration into this approach is needed, but the inclusion of an integrated assessment of pain intensity and rescue use as an outcome variable merits further consideration in defining analgesic activity when rescue medication is part of the study design.

**3. Title:** Drug utilization review of pregabalin and concomitant medication

**Presenter:** Andrew G. Kowal, MD

**Biography:** Dr. Kowal is an anesthesiologist with Lahey Clinic Interventional Pain Management. He completed a pain management fellowship at Johns Hopkins and is board certified in anesthesiology with a subspecialty in pain management.

**Co-presenters:** Virgie Zajac, RN, CRRN, Lahey Clinic Interventional Pain Management Center; Colleen Moffitt, PharmD, Medical Outcomes Specialist at Pfizer, Inc.

**Abstract:**

**Methods:** Pregabalin utilization and its impact on concomitant medication use were assessed via a retrospective evaluation of 387 patients treated at Lahey Clinic Interventional Pain Management Center. Using an e-prescribing database, records were reviewed to assess utilization of pregabalin and concomitant medications for 3 months prior to and after the initiation of therapy. We assumed patients were adherent to all medications. For medications that were prescribed as needed (PRN), we assumed patients took medications at the maximum prescribed quantity and frequency. Daily narcotic utilization was standardized to morphine equivalent units. The use of other concomitant medications was counted as a dichotomous variable, based on the presence of a prescription.

**Results:** The starting daily dose of pregabalin was 150 mg in a majority of patients (63.5%). This was also the last recorded dose for 50% of patients. We observed a significant decline in narcotic use, from 28.7% to 22.0% (p=0.031), and a significant increase in the use of topical lidocaine, from 3.4% to 6.7% (p=0.032). The use of antidepressants, other anticonvulsants, NSAIDs, muscle relaxants, and anxiolytics did not change significantly after the initiation of pregabalin. Of the 111 patients receiving narcotic analgesics prior to initiation of pregabalin, 61.3% experienced a reduction in narcotic use, 23.4% experienced no change and 15.3% experienced an increase in narcotic use. 47 of the 111 patients (42.3%) utilizing narcotics prior to the initiation of pregabalin discontinued use

completely after the initiation of pregabalin. 22 of the 276 patients (8%) who were not utilizing narcotics in the 3-month period prior to pregabalin initiation had narcotics added to therapy after or at the same time pregabalin was initiated.

**Conclusions:** Based on the results of this uncontrolled observational analysis, further investigation of concomitant medication use in pregabalin users in a randomized controlled trial is warranted.

Disclosure: This study was supported by Pfizer, Inc.

**4. Title:** Treatment of post-bunionectomy acute pain with HC/APAP CR

**Presenter:** Michael H. Golf, DPM, PA

**Biography:** Dr. Golf is a podiatrist in private practice in Austin, Texas, with research facilities in conjunction with Scirex for bunionectomy studies in Austin and Houston.

**Co-presenters:** Mark McDonnell, DPM, FACFAS, podiatrist at Hill Country Sports Medicine of Podiatric Surgery and at Texas State University, San Marcos; Stanton M. Smith, DPM, private-practice podiatrist in Murray, UT, SCIREX, Foot and Ankle Institute/Arlington Park Surgery Center in Salt Lake City; James W. Thomas, MS, Manager of Statistics at Abbott; Earle Lockhart, MD, Senior Medical Director of Pain Care at Abbott; Andrea Erickson Best, DO, MPH, Global Project Head of Pain Research and Development at Abbott; Rita I. Jain, MD, Divisional Vice President of Pain, Respiratory, and Metabolic Development at Abbott



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## **Abstract:**

**Objective:** To compare the safety and efficacy of a 12-hour extended-release hydrocodone 15 mg/acetaminophen 500 mg (HC/APAP CR) formulation given as a single dose, as well as that of a short-acting hydrocodone 10 mg/acetaminophen 325 mg (HC/APAP IR) formulation dosed every 4 hours for 3 doses, with placebo in patients with moderate-to-severe pain on the day following primary, unilateral, first metatarsal bunionectomy surgery (ICD-9 code 729.5).

**Methods:** Patients were randomized to one dose of 2 tablets HC/APAP CR (n=29), or one tablet HC/APAP IR (n=31) every 4 hours for 3 doses, or placebo (n=31) and assessed for 12 hours. The primary endpoint was the time-interval weighted sum of pain intensity difference (SPID) for 0 to 12 h following initial drug administration using 100 mm VAS. Secondary endpoints included SPID categorical scale (0 to 12 h), time-interval weighted sum of pain relief (TOTPAR, 0 to 12 h) and pain relief and pain intensity difference (SPRID). Safety assessment included adverse event (AE) monitoring.

**Results:** Baseline characteristics were similar among treatment groups. Mean SPID (0 to 12h) scores were statistically superior for HC/APAP CR (333) and HC/APAP IR (242) compared with placebo (20.7). Mean SPID categorical, TOTPAR, and SPRID scores for HC/APAP treatment groups were also significantly higher statistically when compared with placebo. Treatment-emergent AEs experienced by  $\geq 5\%$  of patients in either HC/APAP treatment group included nausea, vomiting, headache, dizziness, somnolence, fatigue, and hypotension. No serious AEs were reported during the study.

**Conclusions:** For postoperative pain, HC/APAP CR and HC/APAP IR were significantly superior to placebo in providing effective pain relief. Overall AE rates with each were not statistically significantly higher than with placebo and were consistent with those of a mu-opioid-containing analgesic.

**Disclosure:** This study was supported by Abbott Laboratories.

**5. Title:** Diclofenac soft gelatin capsules for postbunionectomy pain

**Presenter:** Stephen E. Daniels, DO

**Biography:** Dr. Daniels is Executive Medical Director for the Clinical Research Centers, Premier Research Group, LTD in Austin, Texas. He has more than 14 years of experience in clinical research and has served as Principal Investigator for more than 200 trials in analgesia and general medicine.

**Co-presenters:** Douglas R. Baum, MS, Vice President, Global Corporate Development, Premier Research Group, LTD; Stephen Boesing, MS, Xanodyne Pharmaceuticals, Inc.

**Abstract:**

**Background:** DPSGC 25 mg is a low-dose, rapidly absorbed soft gelatin capsule formulation of diclofenac potassium under development for the treatment of mild-to-moderate pain.

**Objective:** To investigate the efficacy and safety of DPSGC 25 mg in a phase 3, multicenter, randomized, double-blind, parallel group, placebo-controlled study in patients with pain following first metatarsal bunionectomy (n=200).

**Methods:** Patients experiencing a requisite level of pain ( $\geq 4$  based on an 11-point numeric pain rating scale [NPRS]; 0=no pain, 10=worst pain possible) on the day following surgery were randomized to DPSGC 25 mg or placebo. Patients requested the second study drug dose (remedication) when needed to treat their pain. Patients were then dosed every 6 hours during the multi-day multiple-dosing period. The primary efficacy endpoint was average NPRS score over the 48-hour multiple-dose period. Additional measures included assessment of summed pain intensity differences (SPID), mean interval time to rescue medication use, proportion of patients using rescue, and onset of perceptible and meaningful pain relief (two stopwatch method).

**Results:** DPSGC provided a significant improvement in average 48-hour NPRS score over placebo (3.3 vs. 5.7, respectively;  $p < .0001$ ) as well as for SPID (203 vs. 87;  $p < .0001$ ) and mean interval time to rescue medication use (325 vs. 256 min;  $p < .0001$ ). The proportion of patients using rescue medication on day 1 and day 2 was reduced in the DPSGC group compared with placebo (54% vs. 92% on Day 1; 30% vs. 67% on Day 2;  $p < .0001$ ). Patients using DPSGC experienced a faster onset of meaningful pain relief compared with placebo ( $p = .003$ ). DPSGC was well tolerated and no DPSGC patients experienced serious adverse events.

**Conclusions:** These results indicate that low-dose DPSGC was well tolerated and efficacious in patients with pain following bunionectomy surgery.

**Disclosure:** This study was supported by Xanodyne Pharmaceuticals, Inc.

## **Art and Music Therapy**

**6. Title:** The effect of music therapy on perceptions of pain in African American and Caucasian patients with chronic nonmalignant pain

**Presenter:** Sandra L. Siedlecki, PhD, RN, CNS

**Biography:** Dr. Siedlecki, a Senior Nurse Researcher at Cleveland Clinic, obtained her PhD from CWRU in 2005. She has over 30 years experience as a clinician, educator, and researcher.

**Abstract:**

**Background:** Although the incidence of arthritis and chronic back pain (CBP), the most common chronic disorders in the US and the leading causes of disability in working age adults, do not differ significantly by race, African Americans have a higher incidence of disability than Caucasians related to these chronic disorders (HP 2010).

**Objective:** To evaluate potential racial variations in response to interventions for the management of chronic nonmalignant pain (CNMP), including the examination of racial variations in response to music therapy.

**Methods:** Secondary analysis of data from a music-pain study previously reported (1), which included African American (n=36) and Caucasian (n=24) CNMP patients, was used to examine racial variations in response to music therapy. Chi-Square and one-way analysis of variance (ANOVA) procedures were used to examine differences at baseline; and multivariate analysis (2X2 MANCOVA)

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was used to determine if there was a difference between African American and Caucasian patients who used music versus those who did not.

**Results:** Overall, music was found to be effective in reducing pain. However, when African American and Caucasian groups were examined independently, differences between music and control in the Caucasian group were significant [ $F(2,19)=5.48, p=.013$ ], with no significant differences found between the music and control for African Americans [ $F(3,31)=1.18, p=.319$ ]. The Caucasian music group has 13% less pain posttest than the African American group as measured by the MPQ-SF and 29% less pain as measured by the VAS. Pain decreased from pretest to posttest for both groups, with a 34% reduction in pain as measured by the MPQ-SF in the Caucasian group and an 11% reduction for the African American group.

**Conclusions:** Findings of different levels of effectiveness provide new knowledge of the usefulness of music for pain. Future research should focus on determining which factors account for this variation in response.

## Reference:

1. Siedlecki SL, Good M. Effect of music on power, pain, depression, and disability. *J Adv Nurs.* 2006;54(5):553-562.

**7. Title:** The clinical effects of music therapy in palliative medicine

**Presenter:** Lisa M. Gallagher, MA, MT-BC

**Biography:** Ms. Gallagher is a music therapist at the Cleveland Music School Settlement and The Cleveland Clinic's Horvitz Center for Palliative Medicine.

## Abstract:

**Background:** There are few quantitative studies involving music therapy for individuals with advanced illness.

**Objective:** The purpose of this study was to determine the clinical effects of music therapy on individuals with chronic and/or advanced illnesses and to increase literature on the subject.

**Methods:** The effects of music therapy on 200 patients with chronic and/or advanced illnesses, including malignancies, nonmalignant syndromes, pain disorders, sickle cell disease, aortic aneurysm, Gardner's syndrome, AIDS, CJD, and neurodegenerative diseases were evaluated (59% female, median age=62 years, 29% had musical background). Visual analog scales, the Happy/Sad Faces Assessment Tool, and a behavior scale recorded pre- and post-music therapy scores on standardized data collection forms. A computerized database was used to collect and analyze the data. The Wilcoxon signed-rank test was used to measure the effect of music therapy on anxiety, body movement, facial expression, mood, pain, shortness of breath, and verbalizations.

**Results:** Patient-rated scores for anxiety, depression, mood, pain, and shortness of breath improved significantly ( $p<0.001$ ). Facial expression, movement, and verbalizations all improved significantly ( $p<0.001$ ) following music therapy. Although sleep was included in the behavioral scale, it was only addressed in 12 sessions. No differences in results were found between patients with and without musical backgrounds. Family members were present in 68 of the 200 sessions, with a median number of 1 family member present (range:

1 to 4). Mood scores of family members improved significantly ( $p<0.001$ ), and the only family rating that did not improve post-intervention was anxiety ( $p=0.50$ ). Facial expression and verbalization also improved significantly ( $p<0.001$ ).

**Conclusions:** This is a significant addition to the quantitative literature on music therapy in this unique patient population. Regardless of musical background, music therapy had a significant effect on both patients and families of patients. Our results suggest music therapy is invaluable to palliative medicine.

**8. Title:** The use of metaphor in art making for acceptance and change

**Presenter:** Rachel Braun, MA

**Biography:** Ms. Braun holds a Masters degree in Creative Arts Therapy. She has used art therapy to help people with chronic pain, adult psychiatric inpatients, and at-risk adolescents.

**Co-presenters:** Nancy Gerber, PhD, Director of the Graduate Art Therapy Education at the Hahnemann Creative Arts in Therapy Program of Drexel University; Lynette A. Pujol, PhD, Director of Psychological Services at Jefferson Pain Center, Department of Anesthesiology, Thomas Jefferson Medical College

## Abstract:

**Objective:** To explore how the use of metaphor in art making helps people with chronic pain express the experience of acceptance and change.

**Methods:** Data were collected from the Chronic Pain Acceptance Questionnaire, Pain Stages of Change Questionnaire, the creation of two art tasks, an open-ended responsive interview, a validation interview, and patient medical history. Four people ( $m=2, f=2$ ; Caucasian=2, African American=2; age range: 48 to 61) with chronic neck, back, or neuropathic pain were recruited from an urban area pain center.

**Results:** The results of this study suggest that although each participant's experience of exploring metaphor in art making was unique, common themes can emerge. The use of metaphor in art making was found to help at least 3 of the 4 participants in this study express the concepts of acceptance and change in each of the following ways: 1) by introducing an opportunity for the openness

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to, or avoidance of a situation, including the art making experience; 2) by providing a safe distance with which to face a challenging situation; 3) through the metaphoric objectification of a situation, allowing for assessment, clarity and wise decision-making; 4) by providing the means for communication about the degree to which security and protection are implemented in their lives; 5) by providing a way to explore personal and professional relationships; 6) by providing a way to reflect the influence of past experiences on present and future situations; and 7) through the discovery of a non-linear, meaningful and relaxing mode of expression.

**Conclusions:** Although further research is required, this study suggests that the use of metaphor in art making elicits a wealth of information regarding the concepts of acceptance and change with people who experience chronic pain, and may prove to be an affordable and beneficial clinical evaluative tool with which to assess treatment goals.

## Back and Spine

**9. Title:** Safety and accuracy of lumbar epidural steroid injection (LESI) in the treatment of radiculopathy

**Presenter:** Saeid Alemo, MD

**Biography:** Dr. Alemo is an American board-certified neurosurgeon in practice for 25 years, who is currently practicing neurosurgery and pain management at Hahnemann University Hospital and Nazareth Hospital in Philadelphia.

**Co-presenter:** Amirali Sayadipour, MD, Co-investigator at the University Neurosurgical Pain Clinic of Nazareth Hospital, Philadelphia,

**Abstract:**

**Background:** The technique of LESI has been a matter of practitioners' preferences.

**Objective:** To assess the safety and accuracy of LESI.

**Methods:** This is a retrospective study of 371 cases who had LESI. Each patient had clinical and imaging evidence of radiculopathy. There were 134 male (36%) and 237 female (64%). Range of age was from 18 to 89 years (mean 52.7 years). The procedure was carried out under Monitored Anesthesia Care. Fluoroscopy and Loss of Resistance (LOR) were used for locating the needle. For confirmation of epidural injection, we injected 0.5 cc of Iopamidol contrast medium. Each patient received 5 cc of 0.25% bupivacaine mixed with 80 mg of methylprednisolone.

**Results:** We detected false LOR in 10.7% of our patients by Iopamidol injection. The procedure was found relatively safe; however, certain rare potential complications such as meningitis, epidural hematoma, epidural abscess, epidural lipomatosis, subdural hematoma, allergic reaction to Iopamidol, weight gain, steroid myopathy, hypersensitivity to steroid (hypertension and tachycardia), avascular necrosis of bone, osteoporosis, fluid retention, Cushing syndrome, hypercorticism, chemical meningitis due to steroid, nerve root injury, arachnoiditis, retinal hemorrhage, acute retinal necrosis, pneumocephalus, transient blindness and death or brain injury were not seen in our series. Our total morbidity was 5.1% which includes: cerebrospinal fluid (CSF) leak (12) that caused transient

headache, transient paraplegia due to incidental intrathecal bupivacaine with full recovery in 6 to 8 hours (5), steroid allergy (1), and hyperglycemia (1).

**Conclusions:** We strongly recommend all patients with lumbar radiculopathy be treated with LESI before considering spinal surgery, except for those that have progressive motor deficit or cauda equina compression requiring urgent spinal surgery. Based on 10.7% of false LOR and potentially serious complications, we believe LOR technique along with an image intensifier and Iopamidol injection in the sterile operation room is the gold standard technique.

**10. Title:** Effects of percutaneous vs. transcutaneous electrotherapy on low back pain

**Presenter:** Edward Workman, MD, EdD, FAAPM, ACFP

**Biography:** Dr. Workman is Medical Director of Neuropsychiatric Pain Medicine Associates of Tennessee; clinical associate professor in the department of medicine at the University of Tennessee Medical Center-Knoxville; and President and CEO of Forensic Medicine Associates, Inc.

**Co-presenters:** Nichole Harness, LPN, Clinical Nursing LPN at Neuropsychiatric Pain Medicine Associates; Jackie L. Hendrix, BS, RN, RT, CCM, CLNC, Executive Vice President of Neuropsychiatric Pain Medicine Associates

**Abstract:**

**Background:** Standard transcutaneous electrical nerve stimulation (TENS) is a widely-used modality in chronic pain, but is limited by the extent to which electrical energy is transferred to pain generation sites. Percutaneous neuromodulation therapy (PNT) uses needle electrodes to set up a deeper electrical current.

**Objective:** This study compares the efficacy of PNT and TENS on pain ratings and social activity of chronic back pain patients.

**Methods:** Subjects included 30 back surgery patients. 10 subjects were randomly assigned to PNT or TENS. Both groups received 10 weekly sessions, using constant stimulus intensity. 10 additional patients were randomly selected from patients in a University-affiliated clinic; they received individualized PNT with regular changes in intensity levels of electrical stimulation. Dependent Variables (DVs) included pre- and post-treatment average pain levels (0 to 10 ratings) and pre/post measures of social activity level.

**Results:** DVs were analyzed via analysis of variance with post HOC Bonferroni follow up tests and simple t-tests. The individualized PNT group exhibited significantly greater pain reduction than the placebo group ( $F=5.7$ ,  $p<.05$ ; Bonferroni  $t=3.36$ ,  $p<.05$ ). No other significant differences were found on the pain DV. Individualized PNT resulted in a 42% reduction in average pain ratings, while the standardized PNT group produced a 24% reduction. The TENS group produced no change in pain ratings. On the social activity DV, the PNT group produced significantly greater improvement in social activity, as compared to the Placebo/TENS group ( $T=3.39$ ;  $p<.01$ ).

**Conclusion:** PNT is more effective than TENS, if individualized. Social activity is improved with PNT but not TENS. Anecdotal evidence, and some of the data, strongly suggests that PNT is particularly efficacious with fusion patients. Further research is needed to investigate this hypothesis.

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**11. Title:** Tramadol ER improves sleep and function in low back pain

**Presenter:** Daniel Ng, PharmD

**Biography:** Dr. Ng is Manager of Regional Outcomes Research for Johnson and Johnson. He holds a Doctor of Pharmacy degree from the University of Illinois at Chicago.

**Co-presenters:** Carmela J. Benson, MS, Associate Director of Outcomes Research, Internal Medicine, Ortho-McNeil Janssen Scientific Affairs; Kavita L. Gajria, BSPharm, MS, Lead Health Economist/Outcomes Scientist, Abt Bio-Pharma Solutions, Inc.; Mark R. Kosinski, Senior Scientist and Director of Consulting Division for QualityMetric, Inc.; John D. Freedman, MD, MBA, Associate Medical Director at the Tufts Healthcare Institute, Adjunct Assistant Professor of Medicine at Tufts University School of Medicine; Jeff R. Schein, DrPH, MPH, Senior Director, Outcomes Research, Ortho-McNeil Janssen Scientific Affairs

**Abstract:**

**Background:** According to the 1999 National Pain Survey, low back pain (LBP) was the most common type of non-cancer-related pain treated by physicians (1). In patients with chronic LBP, higher pain intensity has been associated with increased sleep disturbance, shorter sleep duration, delayed sleep onset, and diminished sleep satisfaction (2).

**Objective:** The efficacy and safety of tramadol ER (Ultram ER; tramadol extended-release) for treatment of chronic LBP were evaluated in a randomized, double-blind, placebo-controlled study following an open-label run-in.

**Methods:** Adults with chronic ( $\geq 6$  months) LBP measuring  $\geq 40$  mm on a 100 mm visual analog scale (VAS; 0=no pain, 100=excruciating pain) were enrolled in the 3-week run-in, during which tramadol ER was titrated to 300 mg once daily (QD). Patients completing run-in were randomized to placebo or tramadol ER 200 mg or 300 mg QD for 12 weeks. Previous pain intensity, pain-related sleep disturbance, and disability were assessed using the VAS, the Sleep Problems Index (0=no disturbance, 100=most disturbance), and the Roland Disability Index (RDI; 0=no impairment, 24=most impairment), respectively. Post hoc trend and responder analyses were performed, the latter to determine the prevalence of clinically meaningful improvement (CMI; ie,  $\geq 30\%$ ,  $\geq 16$  mm, and  $\geq 50\%$  reduction, respectively, in pain intensity, Sleep Problems Index, and RDI) in each outcome from baseline to Week 12 in each group. 386 were randomized to 200 mg (n=129), 300 mg (n=128), or placebo (n=129).

**Results:** Trend analyses demonstrated improvements in all outcomes during run-in and were better maintained by the tramadol ER groups during the double-blind phase, with significant separation from placebo at Week 1 in all parameters for 300 mg and in pain intensity and Sleep Problems Index for 200 mg (all  $p < 0.05$ ). A significantly higher percentage of patients in the 300 mg group achieved CMI in pain intensity (71.1%), Sleep Problems Index (64.8%), and RDI (46.1%) compared with the placebo group (51.6%, 51.7%, and 32.0%, respectively; all  $p < 0.05$ ). A higher percentage of patients receiving 300 mg (75.8%) versus placebo (55.8%;  $p < 0.003$ ) experienced  $\geq 1$  adverse event during the double-blind period.

**Conclusions:** In summary, tramadol ER 300 mg was associated with clinically meaningful improvement in pain intensity, pain-related sleep disturbances, and disability in patients with moderate-to-severe chronic LBP.

**References:**

1. Ortho-McNeil Pharmaceutical. 1999 National Pain Survey: Executive Summary. Available at: [http://www.chiro.org/LINKS/FULL/1999\\_National\\_Pain\\_Survey.html](http://www.chiro.org/LINKS/FULL/1999_National_Pain_Survey.html). Accessed July 10, 2007.
2. Cohen MJM, Menefee LA, Doghramji K, et al. Sleep in chronic pain: problems and treatments. *Int Rev Psychiatry*. 2000;12:115-126.

**Disclosure:** This study was supported by Ortho-McNeil Janssen Scientific Affairs.

**12. Title:** Effectiveness and safety of buprenorphine transdermal system (BTDS) compared with hydrocodone/acetaminophen in the treatment of patients with chronic low back pain

**Presenter:** Catherine L. Munera, PhD

**Biography:** Dr. Munera has been working in the pharmaceutical industry for 20 years. She is currently the Director of Statistics and Statistical Programming at Purdue Pharma LP.

**Co-presenters:** Martin Hale, MD, Gold Coast Research, LLC; Daniel A. Spyker, MD, Vice President, Alexza Pharmaceuticals; Curtis Wright IV, MD, Senior Vice President, Star Scientific, Inc.

**Abstract:**

**Objective:** To compare the effectiveness and safety of BTDS, a 7-day matrix transdermal system containing buprenorphine, a partial mu-opioid agonist, to hydrocodone/acetaminophen (HCD/APAP) tablets, a widely-prescribed opioid combination product, in patients with chronic low back pain.

**Methods:** 270 patients were enrolled in a randomized, double-blind, multiple-dose, active-controlled, long-term (56 day) study. During a 7-day run-in period, patients discontinued all analgesics and took 400 mg ibuprofen qid, which they continued throughout the study. During the first 21 days, patients titrated to an effective level of analgesia (3 dosage levels: BTDS 5, BTDS 10, or BTDS 20 [5 mcg/h, 10 mcg/h, or 20 mcg/h, respectively]; applied every 7 days, or HCD/APAP [2.5 mg hydrocodone/250 mg acetaminophen; 1, 2, or 3 tablets qid]). Patients continued on an acceptable effective dose for the 35-day maintenance period. Baseline pain scores for "average pain intensity over the last 24 hours" (0 to 10 scale) were similar for the BTDS (7.74) and HCD/APAP (7.65) groups (difference, 0.09; 95% confidence interval [CI], -0.27 to 0.44).

**Results:** Efficacy: Mean average pain intensity for the maintenance period was similar for BTDS (5.96) and HCD/APAP (6.04) (difference, -0.08; 95% CI, -0.60 to 0.44). The effect of BTDS on pain intensity was indirectly compared to placebo using a meta-analysis of published HCD vs. placebo literature (n=7) and was significantly different ( $p < .0001$ ). For the global satisfaction question, "How would you rate the study medication you received for pain?" (0 to 4 scale), the mean for the maintenance period was similar for BTDS and HCD/APAP (difference, 0.16; 95% CI, -0.08 to 0.39).

**Safety:** Safety measures, including adverse events, clinical laboratory tests, and vital signs, showed a similar safety profile between BTDS and HCD/APAP.

**Conclusions:** BTDS was shown to be as effective and safe as HCD/APAP in this long-term study in patients with chronic low back pain. (Encore Presentation)

**Disclosure:** This study was supported by Purdue Pharma LP.

**13. Title:** Efficacy and safety of duloxetine 60 mg to 120 mg once daily in patients with chronic low back pain

**Presenter:** Ellen Schoenberger, BS

**Biography:** Ms. Schoenberger is a Neuroscience Medical Liaison with Eli Lilly. Ellen received her BS in Pharmacy from the University of Illinois, and was with The Upjohn Company in various medical and marketing positions before joining Eli Lilly.

**Co-presenters:** Vladimir Skljarevski, MD, Clinical Research Physician at Eli Lilly; Durisala Desai, PhD, Communications Consultant at Eli Lilly; Hong Liu-Seifert, PhD, Research Scientist at Eli Lilly; Qi Zhang, PhD, Research Scientist at Eli Lilly; J. Hampton Atkinson, VA San Diego Healthcare System; Miroslav "Misha" Backonja, MD, professor of Neurology, Anesthesiology, and Rehabilitation Medicine at the University of Wisconsin

**Abstract:**

**Background:** Chronic low back pain (CLBP) is a common musculoskeletal disorder of complex and not fully understood pathophysiology. By modulating pain inhibitory pathways, duloxetine has been shown to be efficacious in reducing pain associated with diabetic peripheral neuropathy and fibromyalgia.

**Objective:** To assess the efficacy of duloxetine in the reduction of CLBP.

**Methods:** Adult patients with a history of non-neuropathic CLBP for > 6 months (n=238), with a weekly mean 24-hour average pain score  $\geq 4$  at baseline (0 to 10 scale), and without major depressive disorder, were treated with duloxetine 60-120 mg once daily for 13 weeks in a randomized placebo-controlled trial. After 7 weeks of duloxetine treatment, patients reporting < 30% pain reduction (nonresponders) had their dose increased to 120 mg. Responders continued on 60 mg. The primary objective was the reduction of the Brief Pain Inventory (BPI) 24-hour average pain score. Secondary measures included RMDQ-24, PGI-I, BPI-S and BPI-I, diary-based weekly mean of the 24-hour average pain score, CGI-S, and response rates. Health outcomes, safety, and tolerability were also assessed.

**Results:** Compared with placebo-treated patients, duloxetine-treated patients had significantly greater reduction in BPI 24-hour average pain scores from baseline (p=.004 at week 13) and in the diary-based weekly mean of 24-hour average pain scores (p=.001 at week 13). Also compared with placebo group, duloxetine group significantly improved on PGI-I, RMDQ-24, BPI-S and BPI-I, diary-based night pain and worst pain, CGI-S, response rates, and SF-36. Significantly more patients in duloxetine group discontinued due to adverse events (p=.047). Most common treatment-emergent adverse events (5%) in duloxetine group included nausea, dry mouth, fatigue, diarrhea, hyperhidrosis, dizziness, and constipation.

**Conclusions:** Compared with placebo, duloxetine 60-120mg once daily significantly reduced pain, improved functioning, and was well tolerated in patients with CLBP.

**Disclosure:** This study was supported by Eli Lilly and Company.

**14. Title:** Carisoprodol 250 mg tablet improves acute lower back spasm

**Presenter:** Gregory Serfer, DO

**Biography:** Dr. Serfer is licensed in internal medicine in Florida, a member of the American Medical Association, is currently head of the South Florida Clinical Research Center in Hollywood, FL, and served as Principal Investigator for this study.

**Co-presenters:** William Wheeler, PhD, Director of Medical Communications for MedPointe/Meda Pharmaceuticals; Larry Gever, PharmD, Director of Medical Information of Medical Affairs for Meda Pharmaceuticals

**Abstract:**

**Objective:** Two double-blind, placebo-controlled trials (Study No.1, MP 505; Study No. 2, MP 502) were conducted to assess the efficacy of a 250 mg qid carisoprodol dosage and to evaluate differences in efficacy among patient subgroups.

**Methods:** The study population consisted of patients with moderate-to-severe, acute lower back spasm. Patients received carisoprodol 250 mg tablets (n=548) or placebo (n=560) qid for a 7-day double-blind treatment period. Efficacy consisted of two co-primary variables: (1) patient-rated relief from starting backache and (2) patient-rated global impression of change. Symptom improvement relative to onset of pain also was evaluated.

**Results:** The co-primary variables improved in both studies (p<.01) with carisoprodol 250 mg compared to placebo at Day 3 (primary analysis). Significant improvements (p<.01) in the co-primary variables occurred in patients 18 to 40; 41 to 60; and > 60 years, with no significant differences among the age groups. Males and females experienced significant improvement, although a greater percentage (p=.04) of females improved in study No.1 for relief of starting backache. For both co-primary variables, patients improved (p<.001) regardless of study entry 1, 2, or 3 days following onset of pain. The most commonly reported adverse events (carisoprodol vs placebo) were drowsiness (13% vs. 6%), dizziness (8% vs. 2%), and headache (5% vs. 2%).

**Conclusions:** These studies demonstrated that patients with acute lower back spasm significantly improved with carisoprodol 250 mg tablets compared to placebo. Subgroup analyses indicated overall similarity in response by demographic and clinical characteristics. Although a statistical difference favoring females for relief from starting backache was observed in one study, the clinical relevance of this finding is not clear.

**Disclosure:** This study was supported by Meda Pharmaceuticals.

**15. Title:** Dose-escalation, placebo-controlled, local histopathology following intraligamentous lumbosacral injections in swine of a pharmacologic agent commonly used in prolotherapy for low back pain

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**Presenter:** Simon Dagenais, DC

**Biography:** Dr. Dagenais is Research Director at the CAM Research Institute and Assistant Professor of Medicine at the University of Ottawa.

**Co-presenters:** John Mayer, DC, PhD, Consultant at CAM Research Institute and Assistant Professor of Medicine at University of South Florida; Scott Haldeman, DC, MD, PhD, Professor of Medicine at University of California, Irvine and Los Angeles; Mark Hite, ScD, DABT, Consultant toxicologist; James Wooley, DC, President of CAM Research Institute.

**Abstract:**

**Background:** Proliferol, a pharmacologic agent commonly used in prolotherapy for chronic low back pain, contains lidocaine hydrochloride 0.25%, dextrose 12.5%, glycerin 12.5%, and phenol 1.0%. Despite extensive clinical experience in humans with this formulation, little is known about its local histopathology effects on the lumbosacral ligaments and other soft tissues adjacent to the injection sites.

**Objective:** To assess the local histopathology effects of proliferol following intraligamentous lumbosacral injections.

**Methods:** Swine were randomly assigned to 4 study groups (6 males/6 females per group): (1) high-dose placebo (0.9% saline); (2) low dose; (3) medium dose; (4) high dose. The low dose was 0.25 mL/kg, equivalent to 20 mL in an 80 kg human (1X); the medium dose was 5X, and the high dose was 10X. Injections were made into the interspinous, supraspinous, sacroiliac, sacrotuberous, and iliolumbar ligaments, as well as the intra-articular facet joint capsules, and sacroiliac ligaments and joints to mimic current clinical use in humans. Tissue samples of the L4-L5 and L5-L6 interspinous ligaments, as well as the sacroiliac ligaments, were examined in all groups.

**Results:** At 24 hours, there were microscopic findings of minimal-to-moderate subcutaneous hemorrhage, as well as inflammation and necrosis in the L4-L5 and L5-L6 interspinous ligaments and adjacent skeletal muscle, which were most evident in the medium and high dose groups. After 14 days of recovery, there remained substantial subacute or granulomatous inflammation and degeneration in the L4-L5 and L5-L6 interspinous ligaments and adjacent skeletal muscle, as well as vascular inflammation or fibrinoid degeneration in adjacent arteries.

**Conclusions:** Injections of 5X and 10X, the human clinical dose of proliferol in lumbosacral ligaments of swine, elicited localized acute inflammatory soft tissue changes at the injection sites after 24 hours, with subsequent evidence of soft tissue repair after 14 days of recovery. These histopathology findings are consistent with the proposed mechanism of action for this intervention.

**16. Title:** Musculoskeletal diagnostic imaging guidelines:

Introduction

Presenter: John A.M. Taylor, DC

**Biography:** Dr. Taylor is professor and coordinator of diagnostic imaging in the chiropractic program at D'Youville College, Buffalo, NY.

**Co-presenters:** André Bussi eres DC, MSc, FCCS (C), D epartement Chiropratique, Universit e du Qu ebec   Trois-Rivi eres; Cynthia K.

Peterson, Professor and Chairperson of the Department of Radiology and Chief of Clinical Radiology at Canadian Memorial Chiropractic College

**Abstract:**

**Background:** Imaging technology can improve patient outcomes by allowing greater precision in diagnosing and treating patients.

However, there is evidence that overuse, under use, and misuse of imaging services occur.

**Objective:** To develop evidence-based diagnostic imaging practice guidelines for musculoskeletal complaints for use by healthcare professionals.

**Methods:** An electronic search of the English and French language literature was conducted. Independent assessment of the quality of the citations used to support recommendations in the guidelines was performed using the QUADAS, the AGREE, and the SPREAD evaluation tools. A first draft of a diagnostic imaging practice guideline was produced, using the European Commission's Referral Guidelines for Imaging document as a template. A modified Delphi process, including 149 international experts, was used to generate consensus on recommendations for diagnostic imaging studies. The reliability of proposed recommendations was further tested on field chiropractors and on a group of specialists both in chiropractic and in medicine in both Canada and the United States. All recommendations were graded according to the strength of the evidence.

**Results:** The research procedure resulted in recommendations for diagnostic imaging guidelines of adult extremity and spine disorders supported by more than 685 primary and secondary citations. High levels of agreement among Delphi panelists were reached for all proposed recommendations. Comments received by specialists were generally very favorable and reflected high levels of agreement with the proposed recommendations, perceived ease of use of guidelines, and implementation feasibility. Part 1 (Lower extremity) resulted in 56 recommendations; Part 2 (Upper extremity) resulted in 32 recommendations; and Part 3 (Spine) resulted in 55 recommendations.

**Conclusions:** These evidence-based guidelines are intended to assist care providers in decision making on the appropriate use of diagnostic imaging for specific clinical presentations. The guidelines are intended to be used in conjunction with sound clinical judgment and experience. Application of these guidelines should help avoid unnecessary radiographs, increase examination precision, and decrease healthcare costs without compromising the quality of care.

## Case Reports

**17. Title:** Case report study: Treatment of 100 cases with the Antalgic-Trak<sup>®</sup>

**Presenter:** Ryan M. Rosenthal, DC

**Biography:** Dr. Rosenthal is the co-director of Advanced Physical Medicine in Oak Park, Illinois. He is a leader in manipulation under anesthesia (MUA) and non-surgical spinal decompression therapy.

**Co-presenter:** Igor Russo, DC, Co-director of Advanced Physical Medicine

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## **Abstract:**

**Background:** Traction decompression is becoming widely used; however, there are few well-designed studies of the technique. There is strong evidence that range of motion therapy is beneficial to improving connective tissue health and relieving pain.

**Objective:** To evaluate the effectiveness of traction decompression combined with range of motion therapy.

**Methods:** 100 patients with acute and chronic low back pain or neck pain, with or without a radicular component, were treated using the Antalgic-Trak®. Kinetic Decompression Mobilization (KDM) allowed the patient's spine to be locked into specific postures. Each case received a total of 20 30-minute treatment sessions over a 6-week period. Patients were scheduled 5 times a week for the first 2 weeks, 3 times a week for the next 2 weeks, and twice a week for the final 2 weeks. Each Antalgic-Trak® treatment was followed by supportive adjunctive therapies. Pain relief was measured using the visual analog scale (VAS).

**Results:** Outcomes indicated 95% success in eliminating pain, or reducing the pain to minimal levels for a variety of spinal conditions. 55 patients experienced complete pain relief with their treatment, and 40 patients reported mild pain (VAS score of 1 to 3). Five patients reported a VAS score higher than 4 after the treatment program. No patients reported worsening of their pain as a result of treatment, and 2 patients went on to have spine surgery.

**Conclusions:** Traction decompression is superior to ordinary traction for pain reduction and restoration of spinal integrity. Because of the Antalgic-Trak®'s positioning capabilities and its "range of motion" technique, clinicians can position the patient's spine in a manner to reduce the stress on tissues and combine these features with traction decompression.

**Disclosure:** Dr. Rosenthal and Dr. Russo did not receive any compensation from the manufacturers of Antalgic-Trak® for conducting this research.

**18. Title:** Epidural haloperidol enhances epidural morphine analgesia: Three case reports

**Presenter:** Paul Sloan, MD

**Biography:** Dr. Sloan is Professor of Anesthesiology, Pain Medicine, and Palliative Medicine with the University of Kentucky.

## **Abstract:**

**Background:** Epidural butyrophenones have been suggested to improve postsurgical analgesia when added to epidural opioids (1).

**Objective:** The purpose of these case studies was to investigate the use of epidural haloperidol to enhance epidural opioid analgesia in patients with postoperative pain.

**Methods:** Mid- or low-thoracic epidural catheters were used for all patients, following negative epidural test doses. All patients received (prior to or during surgery) a mixture of epidural haloperidol 1 mg/morphine 2 mg.

**Results:** Patient 1 was a 63-year-old female with laparotomy for cancer resection. IV fentanyl 200 mcg was the only opioid used during surgery, with no additional epidural analgesics. Despite receiving a basal epidural infusion, she required 9 mls of PCA epidural solution during her first 30 hours postoperatively to achieve

pain relief. Patient 2 was a 56-year-old female for laparotomy. She received no IV opioids or any epidural local anesthetics during surgery or postoperative stay. She remained pain-free post-op, receiving only ibuprofen 600 mg at 36 hr after surgery. Patient 3 was a 51-year-old male for hip surgery. He received IV fentanyl 100 mcg and no epidural local anesthetics during surgery. He awakened pain free from surgery (verbal pain rating score of 0; 0=no pain; 10=worst pain) and required a total of only 9 mls of epidural analgesics for his entire post-op course to achieve pain relief. No untoward side effects were noted in any patient related to epidural haloperidol use.

**Conclusions:** These case reports provide evidence that epidural haloperidol appears to enhance epidural morphine among patients with postoperative pain. Clinical trials to determine efficacy and side effect profiles of epidural haloperidol are clearly indicated.

## **Reference:**

1. Kotake Y, Matsumoto M, Ai K, Morisaki H, Takeda J. Additional droperidol, not butorphanol, augments epidural fentanyl analgesia following anorectal surgery. *J Clin Anesth.* 2000;12(1):9-13.

**19. Title:** Low-dose intrathecal naloxone to enhance intrathecal morphine analgesia: A case report

**Presenter:** Paul Sloan, MD

**Biography:** Dr. Sloan is a professor of Anesthesiology, Pain Medicine, and Palliative Medicine with the University of Kentucky.

## **Abstract:**

**Background:** Ultra low doses of opioid antagonists (naloxone) block excitatory opioid receptor pathways and may paradoxically enhance morphine analgesia.

**Objective:** The purpose of this case study was to evaluate the safety and efficacy of ultra low-dose intrathecal (IT) naloxone added to IT morphine for the treatment of refractory severe chronic low back pain.

**Methods:** A 56-year-old man with a history of severe chronic low back pain (post-laminectomy syndrome) was evaluated. Prior treatments included physical therapy, antidepressants, oral opioid analgesic trials, adjuvant analgesics, steroid epidural injections, lumbar laminectomy, and spinal cord stimulation. Initial therapy at our clinic was a lumbar IT trial of morphine (unsuccessful) up to 50 mg/d. The addition of IT clonidine (up to 75 mcg/d) and ketamine (6 mg/d) were without benefit. With patient consent and approval, we administered an IT bolus of morphine 2 mg combined with IT naloxone 20 ng.

**Results:** The onset of pain relief was within 20 minutes and peaked at 1 hour with a 50% reduction in VAS pain score. The initial IT morphine 2mg/naloxone 20 ng dose was repeated and the patient followed in hospital overnight. There were no signs of adverse drug toxicity or hemodynamic compromise. An IT infusion of daily morphine 5 mg and naloxone 50 ng was started.

**Conclusions:** Throughout the 3-year follow-up period, the patient maintained pain reduction of 60% to 80%, with a return to daily activities and no further hospitalizations.

**20. Title:** Spinal cord stimulator for the treatment of a woman with vulvovaginal burning and deep pelvic pain: A case report

**Presenter:** Vadim Kushnerik, MD

**Biography:** Dr. Kushnerik is currently the Director of Pain Management at New York Downtown Hospital. He graduated from Stony Brook Medical School with distinction in research. He received training in Internal Medicine at Long Island Jewish Medical Center. He received training in Anesthesiology and fellowship in Pain Management at Columbia Presbyterian Medical Center.

**Co-presenter:** Svetlana Zhovtis, MD, resident in the Department of Neurology at Mount Sinai Medical Center in New York

**Abstract:**

**Background:** Vulvodynia is a chronic pain disorder of the vulva that occurs in the absence of visible infectious, inflammatory, neoplastic, or neurological findings. Multiple treatment modalities are used, often with insufficient results. We report the successful use of a spinal cord stimulator to treat vulvodynia symptoms in a patient who had unsuccessful prior conservative therapies.

**Methods:** A postmenopausal woman presented with 15 years of treatment for vulvar and vaginal burning and deep pelvic pain. She had been taking multiple pain medications with inadequate relief. After successful test stimulation, a permanent spinal cord stimulator was implanted.

**Results:** At 10 months post-treatment, her pain improved by 80%, and the patient no longer requires oral medication.

**Conclusion:** The use of spinal cord stimulation was successful in a patient with vulvodynia, who had been unsuccessful with prior conservative therapies, and whose symptoms were diffuse in nature.

**21. Title:** Vertebral body augmentation therapy—at times an urgent need: A case report

**Presenter:** Carey M. Pilo, DO

**Biography:** Dr. Pilo is currently an anesthesiology resident at the University of Massachusetts Medical School, with clinical interests in pain medicine, regional anesthesia, and osteopathic manipulative therapy.

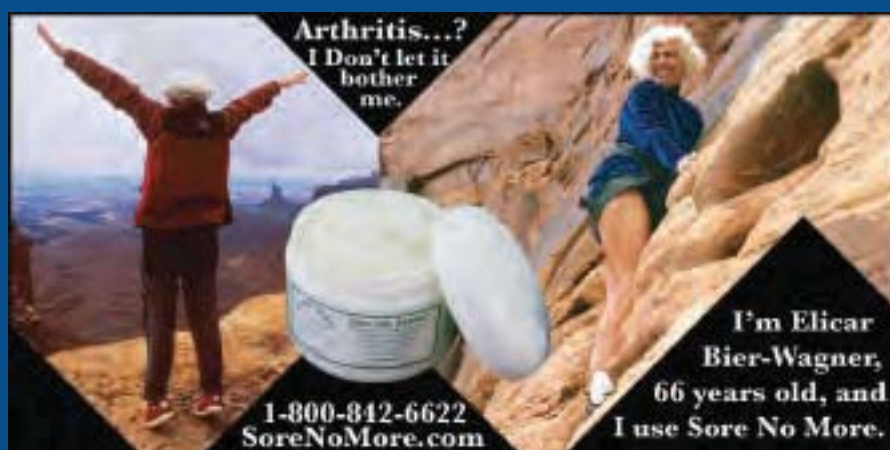
**Co-presenter:** Christian D. González, MD, Director of Pain Services and Assistant Professor at the University of Massachusetts, Worcester

**Abstract:**

**Background:** Vertebral body augmentation therapy is an established, minimally-invasive procedure for vertebral body compression fractures, which is generally reserved for patients with acute and sub-acute fractures that have failed conservative medical therapy. Although this procedure has been performed on an urgent basis within days of the initial injury, it is not well documented in the literature.

**Objective:** To report a case of vertebral body augmentation therapy as an urgent procedure following the failure of medical therapy for pulmonary decompensation.

**Methods:** A 64-year-old woman with a history of severe COPD, home oxygen, CAD status post-stent on anti-platelet therapy, osteoporosis, and chronic low back pain, experienced a sudden, sharp back pain that radiated to her chest. A chest radiograph revealed a new T6 vertebral body compression fracture. Her analgesic and oxygen requirements increased while her mobility



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decreased. On hospital day 5, she developed increasing shortness of breath and was transferred to the ICU for noninvasive ventilation with BiPAP. On hospital day 6, the patient was taken to the operating suite for single-level vertebral body augmentation via kyphoplasty at T6 under monitored anesthesia care.

**Results:** There were no complications to the augmentation and the patient was transferred to the PACU. Back pain decreased from 8/10 to 0-2/10, which was concurrent with a de-escalation of opioids over the same interval. On post-operative day 2, the patient was able to ambulate without assistance for the first time in 7 days. She was discharged 9 days post-operatively.

**Conclusions:** At the time of consultation, significant morbidity and mortality risks were present, including hemorrhage and mechanical ventilation. As the hospital stay progressed, conservative measures were unable to prevent pulmonary decompensation, and operative intervention marked short-term clinical improvement. While this procedure is generally scheduled on an elective basis, the present case provides support for its performance on an urgent basis as dictated by the patient's clinical status.

**22. Title:** Multiple myeloma presenting with thoracic back pain: A case report

**Presenter:** Hoylond Hong, MD

**Biography:** Dr. Hong is Chief Resident (2008-2009) of Physical Medicine and Rehabilitation at the Stanford University School of Medicine.

**Co-presenters:** Henry Lew, MD, PhD, Attending Physician, Physical Medicine and Rehabilitation at Stanford University School of Medicine; Reena Agrawal MD, Resident, Physical Medicine and Rehabilitation at Stanford University School of Medicine

**Abstract:**

**Background:** A 60-year-old male presented at a tertiary care academic medical center with a 4-month history of fatigue and low thoracic non-radiating back pain, aggravated by weight-bearing activity. The pain was increased with standing, walking, and relieved when lying supine.

**Methods:** Physical examination revealed 10% of normal lumbar flexion and 25% of normal lumbar extension. Strength was 4/5 at bilateral hip flexors and normal at all other upper and lower myotomes. Sensation and reflexes were intact and symmetric. Straight leg raising test was negative.

**Results:** Radiographs revealed recent T11 anterior compression fracture. Magnetic resonance imaging showed multiple vertebrae with mottled signal intensity consistent with diffuse metastatic disease and tumor mass at T3 and T11 causing cord compression. Comprehensive evaluation showed findings consistent with metastatic multiple myeloma. The patient was managed with steroids, radiation therapy and chemotherapy. At the time of diagnosis, the patient needed moderate assistance with activities of daily living (ADLs) and maximum assistance with sit to stand transfers. During the patient's cancer treatment, he continued with physical and occupational therapy programs. After four weeks, he improved to minimum assistance with ADLs, sit-to-stand transfers, and was ambulating short distances with a front wheel walker.

**Conclusions:** Multiple myeloma may present with vague symptoms including bone pain, fatigue, weight loss, and fever. Physiatrists treating seemingly musculoskeletal pain should maintain a high index of suspicion for additional underlying pathology. Early diagnosis and treatment of multiple myeloma, coupled with rehabilitation program, can improve function, and contribute to overall quality of life.

**23. Title:** Bilateral meralgia paresthetica in a 60-year-old male with lumbar spinal stenosis: A case report

**Presenters:** Randy L. Calisoff, MD, and Nermeen Aziz, MD

**Biography:** Dr. Calisoff is a PGY 3 Resident in Physical Medicine & Rehabilitation at Loyola University, Maywood, Illinois. Dr. Aziz is an Attending Anesthesiologist at Hines VA Medical Center in Illinois.

**Abstract:**

**Background:** Meralgia paresthetica (MP) is a painful condition often attributed to entrapment or injury to the lateral femoral cutaneous nerve (LFCN), where the nerve leaves the pelvis, manifesting as paresthesia, pain, or numbness in the nerve's distribution. While cases of unilateral MP are more common, bilateral involvement is rare, and has only been reported to occur on average in 15% to 20% of all cases. A literature search failed to reveal any cases of bilateral MP associated with lumbar spinal stenosis.

**Objective:** To describe a unique case of MP in a patient with a history of lumbar spinal stenosis.

**Methods:** A 60-year-old male with a history of lumbar spinal stenosis presented with 2 years of bilateral burning sensations affecting the lateral aspect of his thighs at a Veterans Affairs-affiliated outpatient pain clinic.

**Results:** History revealed that the patient underwent 3 lumbar epidural steroid injections with fluoroscopic guidance in 2007 without pain relief. Medication consisted of 300 mg acetaminophen with 30 mg codeine every 6 hours as needed. Physical examination showed allodynia in the distribution of the LFCN bilaterally and tenderness to palpation of the lumbar paraspinal musculature. The patient was then consented for bilateral LFCN blocks. After localization using a nerve stimulator, each LFCN block was performed with 10 mL of bupivacaine 0.25% with epinephrine 1:200,000 and 20 mg methylprednisolone. The patient tolerated the procedure well and reported immediate pain relief.

**Conclusions:** MP is associated with a range of etiologic factors and can mimic the symptoms of low back pain. Consequently, MP diagnosis can often be misidentified and underdiagnosed, leading to potentially unnecessary procedures and tests for the patient. This case stresses the importance of having a thorough and systemic approach to patients with low back pain in order to eliminate other potential causes.

## Disparities and Perspectives in Care

**24. Title:** A description of ethnic differences in pain assessment and management of patients presenting with long bone fracture in the ED

**Presenter:** Cynthia D. Epps, PhD, RN

**Biography:** Dr. Epps is Professor and Undergraduate Nursing Coordinator at the University of West Georgia. She and colleagues are currently analyzing data from a new study about ethnic disparities in pain management.

**Co-presenter:** Laurie Jowers Ware, PhD, RN, Professor and Coordinator for the Graduate Program in the Department of Nursing at the University of West Georgia

**Abstract:**

**Background:** Although many studies have documented ethnic disparities in analgesia administration, few have dealt with wait time for analgesia in the emergency department (ED), despite the fact that the provision of timely and appropriate analgesia should be a primary goal in caring for patients. Inadequate analgesia has been reported for patients presenting with long bone fractures (LBFs), and a body of evidence exists indicating that ethnic and minority patients may be receiving inadequate pain care when presenting to the ED for treatment of LBFs.

**Objective:** To determine whether wait time differences in pain treatment existed for ethnic and minority adults (18 years or older) who were admitted to the ED with LBFs.

**Methods:** Using a quantitative retrospective design, purposive sampling of 234 Caucasian, African American, and Hispanic of patient medical records presenting with LBFs from 2 small Georgia hospitals were analyzed.

**Results:** Although Hispanic, Caucasian, and African American patients in this study all reported substantial pain, a significant ( $p=.005$ ) overall wait time difference was found between Hispanic and Caucasian patients, with Hispanic patients waiting an average of 102 minutes for the first dose of analgesia, and Caucasians waiting an average of 67 minutes. Significant ( $p=.011$ ) wait time differences were also found between Hispanics and Caucasians when opioids were ordered, and when there was a nurse notation of pain in the record ( $p=.029$ ).

**Conclusions:** Although Hispanic, Caucasian, and African American patients in this study all reported significant pain, Hispanic patients with LBFs had to wait longer for analgesia than Caucasians. Further study is needed to examine the possible causes of the disparity, including study of language barriers and cultural nuances that influence how pain is communicated and assessed by patients, nurses, and physicians, as well as how the healthcare facility, its geographic location, and socioeconomic and access factors influence pain management decisions.

**25. Title:** Community pharmacists' perspective on pain: A 3-year study

**Presenter:** Karen F. Marlowe, PharmD, BCPS, DAAPM

**Biography:** Dr. Marlowe is an Assistant Professor of Internal Medicine at the Auburn University School of Pharmacy and the University of South Alabama School of Medicine. Her research focuses on perceptions related to chronic pain.

**Abstract:**

**Objective:** To assess current perceptions of retail pharmacists in 2 Alabama counties, related to pain management, and to compare the results to those from a previous study conducted over the previous two years.

**Methods:** A 41-question survey was distributed to 100 pharmacists in a 2-county area, including both urban and rural locations, in 2006, 2007, and 2008. Approximately half of the surveys were returned each year. Respondent demographics for each year will be presented. Questions were grouped into several categories, including education regarding pain management, knowledge regarding opiates and NSAIDs, and familiarity with current controlled substance regulations. Other questions asked about the volume of individual medications filled, including CII, CIII and NSAID agents. Pharmacists were asked to indicate their comfort level in discussing individual medications with patients and answering patient questions regarding their chronic pain conditions.

**Results:** Summary data will be presented from each of the question groups. The data will be analyzed for trends across the three years of data as well as for any correlations between the demographic and perspective groups.

**Conclusions:** Responses from this survey will be used to guide the educational efforts of several organizations, to provide targeted continuing education to pharmacists related to chronic pain disease states and their management.

**26. Title:** Evaluation of a pain management education program for RNs

**Presenter:** Judith Wells, RN, BN, MN

**Biography:** Ms. Wells is employed at the Western Regional School of Nursing in Newfoundland, Canada, where she teaches in a four-year Bachelor of Nursing (Collaborative) Program. She is currently lead investigator evaluating the effects of a change in a patient care delivery model on nurses as well as the evaluation of a revised nursing orientation program and a mentorship program for newly nursing graduates.

**Abstract:**

**Background:** It is suggested that the undertreatment of chronic cancer pain is related to poor knowledge and attitudes of nurses and the lack of continuing education related to cancer pain management.

**Objective:** To evaluate the effectiveness of a cancer pain management education program in improving the knowledge and attitudes of registered nurses, and to determine whether the program made any impact in nursing practice.

**Methods:** The Nurses' Knowledge and Attitude Survey (NKAS) regarding pain was used to determine whether the cancer pain management education program was effective in improving knowledge and attitudes. A convenience sample of 27 registered nurses working in a variety of facilities within a regional health board in Newfoundland participated in the study.

**Results:** Analysis of the data revealed a significant improvement ( $p=.000$ ) in scores following program implementation. Evaluation of program content and facilitators was quite positive and, at the 3-month follow-up, nurses reported positive changes in nursing practice that were client focused. There were no significant correlations observed between any study variables. The small convenience sample prevents the ability to generalize the findings, and the subjectivity of the 3-month evaluation with no client perspective is also limiting.

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**Conclusions:** It is concluded that the education program was effective in improving nurses' knowledge and attitudes related to chronic cancer pain management. Based on the results in this study, there may be a need to provide education to all nurses within this regional health board. There is also opportunity to conduct research into implementing best practices guidelines related to pain management and client outcomes. The nursing curricula in schools of nursing need to ensure that new graduates have adequate knowledge of pain management. Finally, organizations must be committed to continuing education, in an effort to improve client outcomes.

**27. Title:** Stolen prescription medication reports: Another viewpoint?

**Presenter:** William J. Granger, MD

**Biography:** Dr. Granger is a part-time pain practitioner in a community hospital and surgery center. He is an anesthesiologist by training and has been in practice 25 years.

**Co-presenter:** Dawn McDonald, BSW, Crime Analyst & Prevention Coordinator for the Marion Police Department in Indiana

**Abstract:**

**Background:** Prescription drug misuse is approaching or exceeding illegal drug use in many parts of the country. Patient reports of filled prescriptions being stolen can be a source of vexation for physicians, and there is a perception among physicians that having the patient report theft to the police will discourage these reports. There is a similar perception among law enforcement officials that these reports are a waste of time, since they are usually bogus.

**Objective:** To determine a more effective protocol for dealing with stolen prescription medication reports.

**Methods:** A local task force was convened with physician and law enforcement representation. A statistician with the police department reviewed 65 stolen prescription reports.

**Results:** Of the 65 reports over a 9-month period, the following facts were revealed: 25% of these victims have their names in the local narcotic intelligence system; 14% have reported medication stolen more than once; 15% have been involved either as victim or witness in an overdose/suicide report; nearly 5% have been suspects in fraudulent prescription cases; 10% have been arrested on OWI (DWI or DUI) or drug-related charges; 26% have been arrested on non-drug-related charges; 62% of reports involve suspicious circumstances; 78% of reports involve one or more of the above items; and 90% of alleged stolen medications were pain/sleep aids/psychiatric medications.

**Conclusions:** These data should make all physicians realize that a report of a drug theft may be the proverbial "tip of the iceberg" and thus a subtle sign of some much deeper medico-psychosocial pathology. Law enforcement officials should realize that these are not just innocuous time-wasting reports, but may represent other ongoing illegal behavior. Clinicians should view these patients as having a high potential for medication misuse and direct their therapy accordingly.

**28. Title:** Pilot project: The chronic pain diary for nursing home residents

**Presenter:** Kathy K. Hager, DNP

**Biography:** Dr. Hager is currently an assistant professor at the Bellarmine Lansing School of Nursing in Louisville, Kentucky. Her experience includes palliative and terminal care and cancer nursing education in the arenas of education, research, and practice.

**Abstract:**

**Background:** Prevalence rates for chronic pain in the nursing home population vary between 45% and 83%, which depends on the resident mental status, demographics, questions asked, assessment methods, and person's willingness to report, among other factors. Research consensus is that the most valid report of pain is that of the person.

**Objective:** To evaluate the use of a self-report diary for assessing chronic pain among nursing home residents.

**Methods:** A one-group pretest and posttest method was used to determine if the use of a pain diary over a 6-week period was associated with changes in pain levels, nursing documentation, and medication use. Baseline data was collected 2 weeks prior to the use of the diary. The diary was used for 2 weeks and data was collected 2 weeks post-intervention. The setting was a 130-bed, not-for-profit facility. Inclusion criteria were documentation of pain, intact cognition (MDS criteria), and ability to communicate (MDS criteria). Of 123 residents in the facility during the project, 53 met inclusion criteria, and 24 of 53 reporting chronic pain. Of these 24, one person declined participation, one died, and one left the facility before project completion.

**Results:** Pain levels, before and after diary use, were comparable to post-intervention data for 7 of the 21 participants. For these 7, the mean pain level increased. The number of pain-related nursing documentation entries before and after use of the diary and the mean number of as needed and scheduled medications per resident also increased, with a significant difference.

**Conclusions:** The diary may be a cost-effective and efficient method for the assessment of chronic pain. There is minimal education required for the person assisting the resident in completing the self-reported diary, and further study could provide information on the time and costs necessary to educate direct care personnel in diary use, and providing assistance to residents in diary completion. Much more persistent pain is present in this population than caregivers realize, and we need a quick and accurate way to define the pain, so that the healthcare professional can have hints that guide pain control. The chronic pain diary could provide that information, at least in the communicative resident population.

## Fibromyalgia

**29. Title:** Pharmacological management of fibromyalgia in UK primary care

**Presenter:** Deirdre Mladsí, BA

**Biography:** Ms. Mladsí has 18 years of experience conducting health economics and outcomes research. Her training is in economics and applied biostatistics, with an emphasis on clinical research.

**Co-presenters:** Melissa Juniper, MS, Director of Health Outcomes Strategy at RTI Health Solutions; Neil Roskell, MSc, Director of Statistics at RTI Health Solutions; Debanjali Mitria, MA, MBA, Associate Director of Health Economics at RTI Health Solutions; Paul Shannon, BSc, Senior Statistical Programmer at RTI Health Solutions; A. G. Wilson, MB, PhD, FRCP, DCH, Head of Academic Rheumatology, University of Sheffield Reader in Molecular Medicine and Rheumatology, Honorary Consultant Rheumatologist; Ana Garcia-Cebrian, Neuroscience Team Leader in the European Health Outcomes Group at Eli Lilly and Company; Trong Kim Le, MPH, Senior Health Outcomes Scientist in Global Outcomes Epidemiology Center of Excellence at Eli Lilly and Company

**Abstract:**

**Objective:** To describe the pharmacological management of patients with fibromyalgia syndrome (FMS) in the United Kingdom.

**Methods:** Pharmacology utilization data from the General Practice Research Database, augmented by costing data from the British National Formulary and the National Health Service Prescription Pricing Authority, were compared for FMS patients and comparison patients.

**Results:** FMS patients (n=8,027) and comparison patients (n=32,108) had a mean age of 48 years. The vast majority (84%) were female, with an average of 6.5 years of available data (over 8 years). Almost all (99.9%) FMS patients had  $\geq 1$  comorbidity; 97.2% of comparison patients had  $\geq 1$  non-FMS diagnosis. Nearly all (99.7%) FMS patients and 94.2% of comparison patients were prescribed  $\geq 1$  pharmacotherapy. Nonsteroidal anti-inflammatory drugs (NSAIDs) (87.5% of FMS patients vs. 54.6 of comparison patients), systemic corticosteroids (75.9% vs. 54.5%), and tricyclic antidepressants (72% vs. 15.5%) were the most commonly prescribed. FMS patients were more likely to be prescribed pharmacotherapies from multiple categories, at any time during the study period (4 to 10 categories; odds ratios [ORs] 2.4 to 21.1) and concurrently (OR 8.3 for  $\geq 2$  categories and OR 7.5 for  $\geq 3$  categories). The annualized cost of pharmacotherapies was £182 per FMS patient and £58 per comparison patient. NSAIDs, centrally-acting analgesics, and systemic corticosteroids were the most expensive pharmacotherapies.

**Conclusions:** FMS patients have greater pharmacotherapy utilization and corresponding economic burden than comparison patients. FMS patients' high multiple and concurrent pharmacotherapy prescribing may reflect the multiple symptoms that characterize FMS.

**Disclosure:** This study was supported by Eli Lilly and Company.

**30. Title:** Milnacipran therapy for fibromyalgia: A 15-week trial

**Presenter:** Philip J. Mease, MD

**Biography:** Dr. Mease is a rheumatologist at Seattle Rheumatology Associates and Swedish Medical Center in Seattle, Washington. He received his MD from Stanford University Medical School.

**Co-presenters:** Daniel J. Clauw, MD, Director of the Michigan Institute for Clinical and Health Research, Associate Dean for Clinical & Translational Research, Professor of Medicine and

Psychiatry, and Director of Chronic Pain & Fatigue Research Center at the University of Michigan; Robert H. Palmer, MD, Senior Director of Forest Laboratories, Inc.; Kim Thacker, MD, Vice President of Medical Affairs at the Forest Research Institute; R. Michael Gendreau, MD, PhD, Vice President of Clinical Development and Chief Medical Officer at Cypress Bioscience, Inc.; Judy F. Gendreau, MD, Clinical Research Consultant and Medical Monitor at Cypress Bioscience, Inc.

**Abstract:**

**Background:** Milnacipran has demonstrated efficacy for treating both the pain and other symptoms associated with fibromyalgia (FM).

**Objective:** This trial was designed to provide further evidence to support the efficacy and safety of milnacipran for treating FM.

**Methods:** Patients meeting ACR fibromyalgia criteria (n=1196) were randomized to placebo (n=401), milnacipran 100 (n=399), or 200 mg/day (n=396) for 15 weeks. Primary efficacy assessments consisted of 2 stringent composite responder analyses. "FM responders" were defined as individuals having  $\geq 30\%$  improvement from baseline in pain (VAS, recorded daily on an electronic Patient Experience Diary [PED]), a rating of "very much improved" or "much improved" on the Patient Global Impression of Change (PGIC) scale, and improvement from baseline of  $> 6$  points in physical function as measured by the SF-36 Physical Component Summary score. "Pain responders" were defined as individuals meeting the above criteria for improvement in pain and PGIC only.

**Results:** At 15 weeks, both milnacipran doses compared to placebo resulted in a statistically significant increase in the number of FM responders (p=.011 and p=.015, 100 and 200 mg/day, respectively). Similarly, response rates for improvement in pain were superior with milnacipran compared to placebo (p=.025 and p=.004, milnacipran 100 and 200 mg/day, respectively). Significant improvements in pain were evident as early as 1 week, and at 3 months, secondary efficacy assessments revealed that milnacipran led to significant improvements on multiple measures of pain: PED morning recall, weekly recall, real-time, and paper VAS measures (p<.05), as well as patient global status: (p<.001), and fatigue (total MFI score). The most-commonly reported adverse events (AEs) were nausea and headache.

**Conclusions:** These findings confirm that milnacipran is a safe and effective treatment for fibromyalgia.

**Disclosure:** This study was supported by Forest Laboratories, Inc. and Cypress Bioscience, Inc.

**31. Title:** Milnacipran has low potential for drug-drug interactions

**Presenter:** Aroon Datta, MSc

**Biography:** Mr. Datta is a Senior Therapeutic Specialist in Psychiatry and Pain with Forest Research Institute (FRI), a Division of Forest Laboratories, Inc.

**Co-presenters:** Antonia Periclou, PhD, Director of Clinical Pharmacology and Drug Dynamics at Forest Research Institute; Stephen M. Coutts, PhD, Director of Pharmaceutical Development at Cypress Bioscience, Inc.; Srinivas G. Rao, Chief Scientific Officer at Cypress Bioscience, Inc.; Robert H. Palmer, MD, Senior Director of Forest Laboratories, Inc.

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## **Abstract:**

**Background:** Milnacipran, a dual serotonin/norepinephrine reuptake inhibitor under investigation for the treatment of fibromyalgia (FM), has been shown to significantly reduce pain and improve other FM symptoms in several clinical trials.

**Objective:** To provide a comprehensive review of milnacipran drug-drug interaction potential.

**Methods:** Ten Phase I drug-drug interaction studies were conducted in healthy subjects receiving single or multiple doses of milnacipran (daily 50 mg, 100 mg, or 200 mg). These studies enrolled between 8 to 28 subjects and ranged from 8 to 52 days in length.

**Results:** The pharmacokinetics of milnacipran were not altered in subjects who were poor metabolizers of sparteine (CYP2D6 deficiency) or mephenytoin (CYP2C19 deficiency) compared to extensive metabolizers. No pharmacokinetic interactions or interaction-related adverse events (AEs) were found with digoxin or warfarin. Milnacipran pharmacokinetics was not altered by either of these drugs. No pharmacokinetic changes were observed with coadministration of either lorazepam or lithium. No clinically significant pharmacokinetic alterations occurred with carbamazepine and levomepromazine. In a study in which healthy subjects switched from fluoxetine to milnacipran without washout, there were no changes in milnacipran pharmacokinetics after single or multiple dosing. In a similar study with clomipramine, the AE profile changed suggesting that patients be monitored when treatment is switched without washout. Finally, milnacipran did not increase motor skill impairment caused by alcohol; alcohol did not affect milnacipran pharmacokinetics.

**Conclusions:** Overall, data from these studies indicate that milnacipran has a low potential for drug-drug interactions and can be safely used with several commonly prescribed medications used by FM patients.

**Disclosure:** This study was supported by Forest Research Institute and Cypress Bioscience, Inc.

**32. Title:** Patient global impression of change in pregabalin fibromyalgia trials

**Presenter:** Jeannette A. Barrett, PhD

**Biography:** Dr. Barrett is Clinical Director with Pfizer Global Pharmaceuticals, New York. She is involved in the development and execution of Phase IIIb/IV clinical development programs with pregabalin.

**Co-presenters:** Lesley Arnold, University of Cincinnati; Teresa Leon, Pfizer Global Pharmaceuticals; Ed Whalen, Pfizer Global Pharmaceuticals; Lynne Pauer, Pfizer Global Research & Development; Bernhardt Zeiher, Pfizer Global Research & Development

## **Abstract:**

**Background:** The Patient Global Impression of Change (PGIC) instrument allows for patients to provide an aggregate measure of their treatment experience.

**Objective:** To identify possible determinants of PGIC response through a pooled analysis of pregabalin treatment studies in fibromyalgia (FM).

**Methods:** 2022 FM patients received pregabalin (150 mg/d, 300 mg/d, 450 mg/d, or 600 mg/d) or placebo in any 1 of 3 double-blind trials of 8 to 14 weeks. Primary efficacy measure in each was endpoint-LOCF mean pain score (MPS, 11-point numeric rating scale [NRS], recorded daily). Sleep quality (11-point NRS, recorded daily), the Multidimensional Assessment of Fatigue (MAF), and the Hospital Anxiety and Depression Scale Anxiety (HADS-A) and Depression (HADS-D) subscales were secondary efficacy measures. Baseline to endpoint changes in scores for each efficacy measure was compared with PGIC response.

**Results:** Pregabalin 300 mg/d, 450 mg/d, and 600 mg/d were associated with significant improvements in MPS: changes from baseline were -1.76, -2.01, -2.08, vs. placebo, -1.25, all  $p < .0001$ . In addition, significant improvements in sleep quality and MAF were observed with 300 mg/d, 450 mg/d, and 600 mg/d; HADS-A with 450 mg/d and 600 mg/d; HADS-D with 450 mg/d. At endpoint, 30.3%, 36.6%, 42.9%, and 42.1% of pregabalin 150 mg/d, 300 mg/d, 450 mg/d, and 600 mg/d patients were PGIC responders vs. 26.4% of placebo patients (300 mg/d, 450 mg/d, 600 mg/d,  $p < .001$ ). Improvement in MPS was most strongly associated with PGIC response: every 1-point improvement in pain was associated with an increase in odds of PGIC response by a factor of 1.92, followed by sleep (1:1.60), HADS-D (1:1.27), HADS-A (1:1.21), MAF (1:1.13).

**Conclusions:** In this large cohort of FM patients, pregabalin was associated with significant improvements in pain, sleep quality, fatigue, and PGIC. Improvements in pain appear to be the strongest driver of PGIC response, followed by improvements in sleep.

**Disclosure:** This study was funded by Pfizer.

**33. Title:** Healthcare utilization by diagnosis stage of fibromyalgia

**Presenter:** Rebecca Robinson, MS

**Biography:** Ms. Robinson is a Principal Research Scientist. Her work includes pharmaco-economic, quality of life, and burden of illness studies in the areas of chronic pain and depression.

**Co-presenters:** Leigh Ann White, PhD, Associate at Analysis Group; Howard G. Birnbaum, PhD, Director of Health Economics Practice and Vice President at Analysis Group; Anna Kaltenboeck, Senior Research Analyst at Analysis Group; Seth Samuels, Analyst at Analysis Group

## **Abstract:**

**Background:** Healthcare use and costs of fibromyalgia (FM) across stage of diagnosis are described.

**Methods:** Two cohorts with 2+ ICD-9 729.1 claims (1999-2005) were selected from insurance claims data: Cohort 1 (newly diagnosed patients) and Cohort 2 (established patients). Annual use and costs (2005 USD) were compared for Cohort 1 pre-diagnosis stage (S1) vs. Cohort 1 post-diagnosis stage (S2), and for S2 vs. Cohort 2 post-index stage (S3), using paired t-tests or nonparametric tests. Cohorts were balanced in age (median 50 years). Cohort 1 had fewer females than Cohort 2 (68.2% vs. 74.0%,  $p < 0.0001$ ).

**Results:** Office visits generally increased across stages: primary care practitioners (S1: 70.9%, S2: 78.3%, S3: 76.3%; all  $p < 0.0001$ ),

chiropractors (S1: 28.8%, S2: 51.1%, S3: 53.3%; all  $p < 0.0001$ ), rheumatologists (S1: 4.2%, S2: 9.9%, S3: 10.5%; S1 vs. S2,  $p < 0.0001$ ; S2 vs. S3,  $p = 0.0595$ ), and non-MD mental health professionals (S1: 6.4%, S2: 7.3%, S3: 8.3%; S1 vs. S2,  $p < 0.0001$ , S2 vs. S3,  $p = 0.0003$ ). Comorbidities were more common in later stages: depressive disorders (S1:12.8%, S2:14.5%, S3:17.3%; all  $p < 0.0001$ ); musculoskeletal pain (S1:46.5%, S2:56.6%, S3:52.9%; all  $p < 0.0001$ ); chronic fatigue syndrome (S1:14.9%, S2:19.2%, S3:17.7%; all  $p < 0.0001$ ). American Pain Society (APS) FM treatment guideline mentioned prescription use increased across stages for SSRIs (20.6%, 22.9%, 25.3%), SNRIs (4.5%, 6.4%, 8.9%), pregabalin/gabapentin (5.4%, 7.4%, 8.8%), benzodiazepines (19.0%, 21.1%, 24.2%), non-benzodiazepine sedatives (9.1%, 11.5%, 13.7%) (all  $p < 0.0001$ ), and opioid analgesics (39.5%, 43.3%, 43.9%; S1 vs. S2), ( $p < 0.0001$ ); (S2 vs. S3,  $p = 0.2835$ ). Use of multiple therapeutic classes increased across stages: patients using 3+ classes (20.1%, 25.0%, 28.0%) and 4+ classes (7.1%, 9.6%, 11.8%; all  $p < 0.0001$ ). Average prescription drug costs increased with stage (S1: \$1,376, S2: \$1,733, S3: \$2,024), as did total healthcare costs (\$6,555, \$8,654, \$8,697; all  $p < 0.0001$ ).

**Conclusions:** Established patients use more medical resources, APS-recommended drugs, and drugs used to treat pain, than those newly diagnosed, and healthcare costs increase in the years following initial diagnosis.

**Disclosure:** This study was supported by Eli Lilly and Company.

**34. Title:** Predictors of duloxetine initiation in fibromyalgia patients

**Presenter:** Rebecca Robinson, MS

**Biography:** Ms. Robinson is a Principal Research Scientist at Eli Lilly. Her work includes pharmaco-economic, quality of life, and burden of illness studies in the areas of chronic pain and depression.

**Co-presenters:** Leigh Ann White, PhD, Associate at Analysis Group; Howard G. Birnbaum, PhD, Director of Health Economics Practice and Vice President at Analysis Group; Anna Kaltenboeck, Senior Research Analyst at Analysis Group; Seth Samuels, Analyst at Analysis Group

**Abstract:**

**Objective:** To investigate factors predicting duloxetine initiation among fibromyalgia patients.

**Methods:** Using Cox proportional hazards models, we investigated effects of baseline health characteristics among fibromyalgia patients on time to duloxetine initiation from the later of index date (duloxetine market entry (08/01/2004)) or first fibromyalgia diagnosis. Characteristics measured in the 6-month pre-index period included demographics, comorbidities, use of medications recommended by American Pain Society (APS), specialty physician services, and fibromyalgia diagnosis stage (newly-diagnosed, established). The sample included 7,965 patients with 2+ fibromyalgia claims (ICD-9 729.1), who were continuously eligible from 02/01/2004 through 12/31/2005. 495 (6.2%) had a prescription for duloxetine during the study period. Time to initiation was measured from index date to the first duloxetine prescription. Observations were right-censored if they did not initiate on duloxetine during the study period. As duloxetine

initiation was strongly associated with established diagnosis, separate models were estimated for 5353 newly-diagnosed and 2612 established patients.

**Results:** For both models, baseline medication use served as the strongest predictor of duloxetine initiation. Use of alpha-2-delta ligands, venlafaxine, SSRIs, TCAs, other antidepressants, opioid analgesics, and non-benzodiazepine sedatives all were strong predictors of initiation (all  $p < 0.05$ ). Dopamine agonists and venlafaxine (hazard ratios: 2.913; 2.338) were the strongest for newly-diagnosed, and alpha-2 delta ligands and SSRIs (hazard ratios: 1.843; 1.819) for the established group. Use of tramadol, female gender, later dates of diagnosis, and chronic fatigue syndrome were significant predictors of duloxetine initiation only among newly-diagnosed patients. Patients seen by chiropractors were less likely to initiate duloxetine. Mental health diagnoses and visits to rheumatologists were significant predictors of duloxetine initiation, only in established patients (hazard ratios: 1.756, 1.476; both  $p < 0.01$ ).

**Conclusions:** Specialty physician use and prior use of APS-recommended drugs are important predictors of duloxetine initiation. Variations in predictors exist for newly-diagnosed and established fibromyalgia patients.

**Disclosure:** This study was supported by Eli Lilly and Company.

**35. Title:** Reliability and validity of the 8-foot Up & Go test as a measure of dynamic balance and functional mobility in persons with fibromyalgia

**Presenter:** Katrina N. Shibata, MPH

**Biography:** Ms. Shibata is recent graduate of the MPH program at California State University, Fullerton. She is also the Research and Program Development Director for the National Fibromyalgia Association.

**Co-presenters:** C. Jessie Jones, PhD, Professor of Health Sciences at California State University, Fullerton, Director of the Fibromyalgia Research and Education Center, and Co-Director of the Center for Successful Aging; Michele Mouttapa, PhD, Assistant Professor in the Kinesiology and Health Sciences Departments at California State University, Fullerton; Jie Weiss, PhD, an Assistant Professor in the Kinesiology and Health Sciences Departments at California State University, Fullerton

**Abstract:**

**Background:** Self-report questionnaires are often used to assess a person's perceived level of physical function. However, a limitation of these instruments is that the underlying physical impairments and functional limitations critical for targeted rehabilitation programs in fibromyalgia (FM) patients are not measured.

**Objective:** To test the reliability and validity of the 8-ft Up & Go as a measure of dynamic balance and functional mobility in a sample of independent, community-residing adults with FM. **Methods:** 56 subjects who met the inclusion criteria for participation in this study, 52 of them (47 women and 5 men), completed the 8-ft Up & Go, FIQ, adapted CPF, and FM Symptom Intensity Rating Scale. **Results:** High test-retest reliability for all participants and for men and women, respectively, were found ( $.93 > R > .997$ ). The

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correlation between the 8-ft Up & Go scores and FIQ scores was moderate for the total sample ( $r=.32$ ), supportive of the convergent validity of the test ( $p<.05$ ). The correlation between the 8-ft Up & Go and CPF scores were considerably higher for total participants ( $r=.74$ ). Furthermore, the 8-ft Up & Go significantly discriminated between people with FM who exercise on a regular basis and those who do not exercise on a regular basis.

**Conclusions:** The results of this study indicate that the 8-ft Up & Go is a quick, easy to use, reliable, and valid measurement tool for clinicians to assess functional mobility in helping to determine appropriate interventions for individuals with FM.

**36. Title:** Effects of topical essential oil on exercise volume after a 12-week exercise program for women with fibromyalgia: A pilot study

**Presenter:** Dana N. Rutledge, PhD, RN

**Biography:** Dr. Rutledge is an Associate Professor of Nursing, and Director of Research for the Fibromyalgia Research and Education Center at California State University, Fullerton

**Co-presenters:** Jessie Jones, PhD, Professor of Health Science and Director of the Fibromyalgia Research and Education Center at CSUF; Nancy Just, BS, Graduate Research Assistant at the Fibromyalgia Research and Education Center, CSUF

**Abstract:**

**Background:** The use of topical analgesics during exercise in people with fibromyalgia (FM) has been understudied.

**Objective:** To determine, in women with FM, the effects of essential oils used with a 12-week exercise program on exercise volume, pain, physical performance, and physical function.

**Methods:** This was a randomized clinical trial comparing 024 essential oil with sham oil combined with exercise. The study included 20 women randomized to 024 oil, 23 to sham oil. Women were trained in oil application (before exercise, at bedtime on exercise days); the 12-week program included weekly group sessions, plus 2 days of home exercise with the recorded regimen. The primary outcome was exercise volume (number of days exercised multiplied by exercise level—intensity and duration). Secondary measures were pain (Brief Pain Inventory), measures of physical performance (30-second chair stands, 6-minute walk, multidimensional balance), and self-reported physical function (Composite Physical Function scale).

**Results:** The average participant was 54 years of age, had some college education, was married, Caucasian, and minimally/mildly depressed. There was no significant difference in exercise volume between women using 024 as compared with those using sham oil after 12 weeks (depression as covariate). There were no significant group nor pre- to post-exercise changes in pain intensity or interference. There were greater positive changes in 30-second chair stands, 6-minute walk distance, and multidimensional balance scores in the 024 group than in the sham group, but these were not significant.

**Conclusions:** The counterirritant 024 oil was not different from the sham oil in its effect on exercise volume (frequency, exercise level—intensity and duration) for women with FM. It is unknown whether 024 actually decreases local pain when used with exercise. Increases

in physical function found, while not significant, may be attributable to the exercise regimen or to the interaction of the oils and exercise regimen.

## Migraine

**37. Title:** The use of opioids for refractory chronic migraine: Efficacy and predictors of success

**Presenter:** Lawrence D. Robbins, MD

**Biography:** Dr. Robbins is a headache specialist and founder of the Robbins Headache Clinic in Northbrook, Illinois. He is also an assistant professor of neurology at Rush Medical College in Chicago.

**Abstract:**

**Background:** Long-acting opioids are one of the available options for those with refractory chronic migraine (CM). Previous studies have demonstrated limited success in this population. While opioids carry some risks, and may be more difficult to prescribe, this patient population has very limited options.

**Objective:** To evaluate the use of long-acting opioids in refractory CM patients.

**Methods:** 115 patients (87F, 28M) were evaluated, with an age range of 23 to 77. Average onset of headaches: 21 years. Medications included long-acting morphine or oxycodone, and methadone. All patients had previously done well on short-acting opioids (although 32 patients had previously overused them) prescribed from 2002 to 2007. Chart reviews and patient interviews were done by the treating neurologist.

**Results:**  $n=115$ . Efficacy: Positive (+) is defined as continuing on the medication at least 9 months, with 40% (or more) improvement in headache (frequency and/or severity). Overall, 65% of patients were + responders. Average years on opioid=4.5 (range 1-13). Results by Age: 23 to 38 yrs:  $n=28$ ; 68% +. 39-59 yrs:  $n=64$ ; 63% +. 60 to 77 yrs:  $n=12$ ; 33% +. Years of headache prior to opioid: 3 to 15 yrs:  $n=37$ ; 69% +. 16 + yrs:  $n=78$ ; 61% +. AEs: 44%; most common AEs were constipation and fatigue. Significant Overuse / Addiction:  $n=32$  (28%). Of these, 91% then overused long-acting opioids. Anxiety:  $n=67$  (58%); 66% +. Overuse in anxious patients:  $n=19$  (28% of anxious patients). Depression (Non-Bipolar):  $n=76$  (66% of total); 68% +. Overuse in depressed (Non-Bipolar) patients: 21 (28% of depressed patients). Bipolar depression:  $n=16$  (14%); 63% +. Overuse in bipolar depression:  $n=5$  (45% of bipolar patients). Working: 75 (65%); 60% +. Overuse in workers: 27%. Disability:  $n=19$  (17%); 63% +. Overuse in disabled patients: 21%.

**Conclusions:** Over a 6-year period, 115 patients with refractory CM were prescribed long-acting opioids. 65% of patients did well for at least 9 months (average 4.5 yrs) on the long-acting opioids, and 44% reported adverse events. Patients more likely to do well included younger patients, high copers, and those without previous opioid overuse. For certain refractory CM patients, long-acting opioids may be beneficial.

**38. Title:** The bipolar spectrum in migraine, cluster, and chronic tension headache

**Presenter:** Lawrence D. Robbins, MD

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**Biography:** Dr. Robbins is a headache specialist and founder of the Robbins Headache Clinic in Northbrook, Illinois. He is also an assistant professor of neurology at Rush Medical College in Chicago.  
**Abstract:**

**Background:** The bipolar spectrum has been shown to occur with increased frequency in migraineurs. Previous studies have primarily focused on bipolar I and II. The current study also includes the “softer, milder” end of the bipolar spectrum. Identifying and recognizing bipolar illness is not simply an academic exercise; the clinical stakes for missing the bipolar diagnosis are enormous.

**Objective:** To evaluate, in addition to migraine, the bipolar spectrum in cluster headache, as well as chronic tension headache (without migraine).

**Methods:** 1200 consecutive migraine patients were evaluated according to DSM-IV guidelines.

**Results:** Bipolar I: 24 Bipolar II: 26, Bipolar NOS: 34 Cyclothymia: 17, Total bipolar spectrum for migraineurs: 103 (8.6%). 287 cluster headache patients were seen over 18 years. Results: Episodic cluster (141): Bipolar I:2 Bipolar II:4 Bipolar NOS: 1 Cyclothymia: 2. Total episodic: 9 (6.4%). Chronic cluster (146): Bipolar I: 2 Bipolar II: 2 (Chronic) Bipolar NOS: 2 Cyclothymia: 4 Total chronic: 10 (6.8%). Total bipolar spectrum for cluster patients: 19 (6.6%). 292 patients with chronic tension type headache, without migraine, were evaluated. Results: Bipolar I:5 Bipolar II:3 Bipolar NOS:3 Cyclothymia:2. Total bipolar spectrum for chronic tension headache: 13 (4.5%).

**Conclusions:** The bipolar spectrum is seen relatively often in headache patients, particularly among migraineurs (8.6%). Cluster headache patients had a slightly lower prevalence of bipolar at 6.6%, and chronic tension headache patients, without migraine, had the least percentage of bipolar at 4.5%.

**39. Title:** The prevalence of personality disorders in migraineurs

**Presenter:** Lawrence D. Robbins, MD

**Biography:** Dr. Robbins is a headache specialist and founder of the Robbins Headache Clinic in Northbrook, Illinois. He is also an assistant professor of neurology at Rush Medical College in Chicago.  
**Abstract:**

**Objective:** To assess 1000 consecutive migraine patients at one headache clinic for Axis II (Personality Disorder [PD]) pathology. The purpose was to determine the prevalence of moderate or severe PD within a headache population.

**Methods:** 1000 patients, 30 to 92 years old, 805 women and 195 men, with IHS diagnosis of migraine, with or without tension headache, were screened. All patients had been assessed via interviews and an intake psychiatric assessment form adapted for headache patients. Diagnosis of PD was done in accordance with DSM-IV criteria. Patients identified as PD fulfilled the criteria, and were also considered moderate or severe; the PD characteristics were pervasive, greatly influencing functioning and social interactions.

**Results:** n=1000. Cluster A PD: Paranoid: 2 (M) .2%; Schizoid: 1 (F) .1%; Schizotypal: 0 Cluster B PD: Antisocial:3 (2M, 1F) .3%; Borderline: 12 (2M,0F) 1.2%; Histrionic: 5 (F) .5%; Narcissistic: 4 (2M, 2F) .4%; Cluster

C PD: Avoidant: 11 (1M, 10F) 1.1%; Dependent: 7 (7F) .7%; Obsessive-compulsive: 7 (7F) .7%; Total PD spectrum (Moderate or Severe): 55/1000 (5.5%); women=46/805(5.7%); men=9/195(4.6%).

**Conclusions:** In this study, 5.5% of migraineurs had a moderate or severe PD. The most commonly seen PDs were borderline (1.2%) and avoidant (1.1%). The recognition of PD greatly affects our approach and management of the pain patient.

**40. Title:** The use of stimulants in chronic migraineurs: Efficacy and predictors of success

**Presenter:** Lawrence D. Robbins, MD

**Biography:** Dr. Robbins is a headache specialist and founder of the Robbins Headache Clinic in Northbrook, Illinois. He is also an assistant professor of neurology at Rush Medical College in Chicago.  
**Abstract:**

**Background:** Several previous studies indicated that stimulants might have utility for CM, as well as for the psychological comorbidities often seen with CM, such as Attention Deficit Disorder (ADD) and depression.

**Objective:** To evaluate the use of stimulants in patients with chronic migraine (CM). The purpose was to determine overall efficacy, and assess which patients may do well with stimulants.

**Methods:** 73 CM patients (57F, 16M) were evaluated, with an age range of 16 to 78. The average onset of headache was 19 years. Lag time after onset of headache prior to the prescription of stimulants was 21 years on average, and they were prescribed stimulants during the 6-year period (2002-2007). Patients who were prescribed stimulants were felt by the neurologist to be good candidates for this class of medication, with low risk for abuse. Fifty-three (53) of 73 patients experienced refractory headache. Retrospective chart reviews and patient interviews were done by the treating neurologist/psychopharmacologist.

**Results:** n=73. Efficacy: To be Positive (+), the patients must have been on the medication for at least 9 months. Fifty-five (55) (75%) of patients continued long-term on the stimulant, for an average of 3 years. Of these patients, 19 (34%) felt that the medication improved headaches at least 50% (frequency and/or intensity). The remaining 36 patients who remained on the medication did so due to other reasons. Results by Age: 16 to 38 years: n=28, 81% +. 39 to 56 years: n=39, 70% +. 60+ years: n=6, 66% +. AES: n=9 (12%). Addiction: n=1, overused/abused the stimulant. Anxiety: n=32, 44% of total. 75% +. Depression (non-bipolar): n=33, 45% of total. 76% +. Bipolar depression: n=14, 19% of total.79% +. ADD: n=24, 33% of total. 92% + long-term. Working: 56 patients were working while on the stimulant. 73% +. Disability: n=6. Only 1 (17%) did well.

**Conclusions:** 75% of the patients remained on the medication and did well for at least 9 months (average of 3 years). They remained on the medication due to improved headache relief (34% had a significant decrease in headache), and/or improvement in comorbid fatigue, ADD, and/or depression. Younger patients and those with ADD were more likely to report positive results. Surprisingly, anxious patients also did well (75%). Stimulants may be helpful for some patients with chronic migraine.

**41. Title:** Migraine treatment with rizatriptan and almotriptan

**Presenter:** X. Henry Hu, MD, MPH, PhD

**Biography:** Dr. Hu received his MD from Shanghai First Medical College and PhD from University of Massachusetts, Amherst. He currently is the Senior Director of Global Outcomes Research & Health Technology Assessment of Merck & Co., Inc.

**Co-presenter:** Daisy Ng-Mak, PhD, Senior Manager of Outcomes Research & Management at Merck & Co., Inc.

**Abstract:**

**Objective:** To compare the effectiveness of rizatriptan 10 mg with almotriptan in routine practice settings.

**Methods:** Migraineurs treated 2 sequential attacks with rizatriptan 10 mg and a usual-care prescription migraine medication in an open-label crossover manner. Patients chose which medication to take first. They recorded treatment outcomes using a stopwatch and a treatment diary. End points included time to onset of headache relief and headache freedom. The Cox proportional hazard model was used to adjust for potential confounding factors (treatment sequence, treatment order, and use of rescue medication).

**Results:** Of 146 patients who took rizatriptan 10 mg and almotriptan as their usual care medication, 79 of them used stopwatches for both attacks. The following analyses were based on responses of these 79 patients. Significantly more patients taking rizatriptan achieved onset of headache relief within 2 hours after dosing than almotriptan (88.6% vs. 73.4%,  $p=0.007$ ). A higher proportion of patients taking rizatriptan achieved headache freedom within 2 hours after dosing than almotriptan (55.7% vs. 45.6%,  $p=0.10$ ). Times to onset of headache relief and headache freedom were significantly shorter with rizatriptan than with almotriptan (median time: 45 vs. 60 min,  $p=0.002$ ; 100 vs. 135 min,  $p=0.004$ , respectively). The adjusted proportional hazard ratios (rizatriptan vs. almotriptan) for times to onset of headache relief and headache freedom were 1.51 (95% CI: 1.20-1.88) and 1.42 (95% CI: 1.15-1.76), respectively. More patients were very satisfied or satisfied with rizatriptan (59.7%) than with almotriptan (56.4%) and fewer patients were dissatisfied or very dissatisfied with rizatriptan (22.1%) than almotriptan (30.8%) and over half of the patients preferred rizatriptan to almotriptan (53.8% vs. 27.9%), with 18.4% expressed no preference.

**Conclusions:** In “real world” settings, migraine patients experienced faster onset of headache relief and headache freedom when they treated their migraines with rizatriptan 10 mg compared with almotriptan.

**Disclosure:** This study was funded by Merck & Co., Inc.

**42. Title:** GERD comorbidity and acute migraine treatment

**Presenter:** X. Henry Hu, MD, MPH, PhD

**First Author Biography:** Božena Katić, MPH, MPA, is a Visiting Research Scientist at Temple University's Center for Pharmaceutical Health Services Research. She provides analytic support to Global Outcomes Research at Merck & Co., Inc.

**Co-presenter:** X. Henry Hu, MD, PhD, Senior Director of Global Outcomes Research & Health Technology Assessment at Merck & Co., Inc.

**Abstract:**

**Background:** GERD (gastroesophageal reflux disease) is a common disorder in the general population, and persistent heartburn is a specific symptom of GERD. NSAIDs and aspirin are widely utilized as acute migraine treatment and can aggravate GERD and associated conditions. Little is known about the co-prevalence of GERD or heartburn among migraineurs and their use of NSAIDs/aspirin-containing medications when treating migraine.

**Methods:** We conducted a web-based survey of migraine patients, and matched responses to a general health survey completed by the same patient within the previous year. The prevalence of diagnosed and symptomatic GERD and heartburn was computed, and the first-line use of prescription and OTC NSAID and aspirin-containing medications during their last migraine attack was tabulated among the diagnosed GERD or heartburn populations, the undiagnosed symptomatic population, and the GERD or heartburn-free population.

**Results:** Of 1832 eligible migraineurs, 403 (22.0%) reported diagnosed GERD, 212 (11.6%) reported diagnosed heartburn, and 290 (15.8%) reported undiagnosed reflux symptoms. A greater proportion of diagnosed GERD/heartburn patients had severe migraines, suffered from chronic daily headaches, had more frequent migraine attacks and had nausea symptoms at headache onset than did the disease-free migraine population. The most common prescription drugs used to treat migraines were triptans (66.7%, 66.2%, 66.9%, and 71.1% for diagnosed GERD, diagnosed heartburn, symptomatic, and disease-free patients, respectively). Prescription and OTC NSAID use was 3.9% and 6.2% among diagnosed GERD patients, 2.9% and 7.2% among diagnosed heartburn patients, 3.9% and 13.9% among undiagnosed patients, and 2.9% and 8.9% among symptom-free migraineurs.

**Conclusions:** We concluded that the prevalence of GERD or heartburn is high among migraine patients. When compared to use by GERD/heartburn-free migraineurs, use of NSAIDs or aspirins as first migraine medication is fairly common among those with diagnosed GERD or heartburn. Physicians should take note of the sizable reflux demographic, and use discretion when prescribing acute migraine medications.

**43. Title:** Tezampanel data suggest peripheral analgesic effect for acute migraine treatment

**Presenter:** Neil M. Kurtz, MD

**Biography:** Dr. Kurtz is the President, Chief Executive Officer, and Board Director of TorreyPines Therapeutics, Inc., the Former President of Ingenix Pharmaceutical Services, and Cofounder of Worldwide Clinical Trials.

**Abstract:**

**Background:** Tezampanel is a nonvasoconstrictive, nonserotonergic, reversible, competitive, and ionotropic glutamate antagonist of the AMPA/kainate subtype. Having demonstrated activity in a variety of preclinical models associated with excitatory amino acid transmission in the CNS, tezampanel is currently in development as a treatment for acute migraine. Historically, subcutaneous injection of sumatriptan has been associated with an approximately 59%

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incidence of injection site reaction. Since it is well-documented that peripheral nerve endings in the skin contain AMPA and kainate receptors, we hypothesized that tezampanel may also exhibit a local analgesic effect.

**Objective:** To assess a local analgesic effect by analyzing the number of patient complaints of injection site pain or burning in a 40 mg tezampanel group compared to a placebo group in a recently-completed Phase II study (1).

**Methods:** A total of 78 patients were randomized to 40 mg tezampanel and 75 patients were randomized to placebo. Using the same diluent, all patients received a single, subcutaneous injection of tezampanel or placebo in the lateral portion of the non-dominant thigh.

**Results:** In the placebo group, 26% (20/75) of patients complained of pain or burning at their injection site compared to 9% (7/78) of the patients who received tezampanel.

**Conclusions:** We hypothesize that by blocking the peripheral AMPA and kainate receptors, tezampanel reduced injection site pain or burning by approximately two-thirds when compared to the placebo group. This finding is supported by data from 3 previous studies in which tezampanel was found to be effective in treating neuropathic pain. Data also suggest that subcutaneous administration of tezampanel should result in less pain or burning to patients than sumatriptan, an important prognostic parameter for better compliance in those migraine patients in which parenteral therapy is warranted.

**Disclosure:** This study was supported by TorreyPines Therapeutics, Inc.

## Reference:

1. Imitrex® Injection (package insert). GlaxoSmithKline: January 2006.

**44. Title:** Treatment of migraine with a sumatriptan auto-injector

**Presenter:** Stephen H. Landy, MD

**Biography:** Dr. Landy is a board-certified neurologist and Headache Medicine specialist, directs the Wesley Headache Clinic and is a Clinical Professor of Neurology at the University of Tennessee Medical School.

**Co-presenters:** Jerome Goldstein, MD, San Francisco Clinical Research Center, President of the Headache and Facial Pain Section of the American Academy of Neurology; Curtis P.Schreiber, MD, Associate Medical Director for the Headache Care Center in Springfield, MO; Jody M. Cleveland, MS, King Pharmaceuticals Research and Development; Richard J. Barrett, PhD, King Pharmaceuticals Research and Development, Kenneth W. Sommerville, MD, Vice-President of Clinical Development at King Pharmaceuticals

## Abstract:

**Background:** An open-label study was conducted at 10 U.S. centers to assess the rate of successful self-injection, pain relief, and tolerability of sumatriptan succinate delivered by a single-use, prefilled, fully pre-assembled auto-injector. The sumatriptan auto-injector delivers 6 mg sumatriptan subcutaneously in 0.5 ml.

**Objective:** The primary endpoint was successful subcutaneous administration of sumatriptan via the auto-injector as demonstrated

by subject report and sponsor inspection of the used auto-injector to confirm activation and delivery. Secondary endpoints included changes in pain scores from baseline to 2-hours post-dose (0-3 Likert scale); preference of the sumatriptan auto-injector vs. prior self-injection of sumatriptan (5-point Likert Scale); and incidence of adverse events (AEs).

**Methods:** The population included males or non-pregnant, non-lactating females of 18 to 60 years of age with 2 migraines per month, with or without aura, and who had prior effective use of subcutaneous injectable sumatriptan. After screening and training, subjects treated themselves as outpatients and returned within 72 hours of treatment for follow-up assessments.

**Results:** 66 subjects (81% female; 95% Caucasian) were screened and 63 were included in intent-to-treat analyses. Of these 63 subjects, 62 successfully self-injected sumatriptan ( $p < 0.001$ ) and reported a decrease in migraine pain from pre- to post-treatment. Sixty subjects (95%) had moderate or severe pain at baseline, and 59 subjects (94%) reported no pain or mild pain 2 hours post-dose. 26 subjects (41%) reported a total of 36 AEs; 31 of 36 (86%) were mild, and 5 were of moderate intensity. The most common AE was mild injection site bruising in 10 subjects (16%). Overall, 41 (65%) of the subjects preferred the new auto-injector, 14 (22%) expressed no preference, and 8 (13%) preferred their previous method of administering subcutaneous sumatriptan.

**Conclusions:** Subjects reported tolerability and migraine pain relief following successful self-administration of sumatriptan with this auto-injector.

**45. Title:** Pre-emption of perimenstrual migraine with frovatriptan

**Presenter:** John Claude Krusz, PhD, MD

**Biography:** Dr. Krusz has a multidisciplinary pain and headache management clinic in Dallas, Texas. He also has clinical interests in sleep, mood disorders, traumatic brain injury, and neuropsychiatric syndromes.

**Co-presenters:** Jane Cagle, LVN, IV Nurse, Anodyne Headache and PainCare; William Knoderer, DDS, MD, Anodyne Headache and PainCare; Stephanie Hall, MPH, Research Coordinator, Anodyne Headache and PainCare; Virginia Scott, BS, Research Coordinator, Anodyne Headache and PainCare

## Abstract:

**Background:** Menstrual migraine can be long-lived and difficult to treat.

**Objective:** To study frovatriptan for the pre-emption of menstrual migraine in a clinic population with this migraine pattern.

**Methods:** 25 women with known menstrual migraines were entered into this open-label study. After baseline history and evaluation, they took 10 mg frovatriptan on Day 1 and 7.5 mg on Day 2 to Day 6, beginning with Day -3 of expected menstrual migraine. They kept headache and HIT6 score diaries. Three menstrual cycles of data were obtained with frovatriptan treatment in this study.

**Results:** Results showed the number of migraine headaches experienced were significantly reduced (4.56 to 1.52 headache days per perimenstrual period),  $p < .001$ , 2 tailed t-test. Perimenstrual migraine severity was also significantly reduced (7.4 to 4.46/10) to

$p < .001$  or less. Four patients were dropped from the study for noncompliance and not for side effects. With respect to the secondary endpoint, HIT6 scores were also significantly reduced (65.1 to 62.7) in each of the 3 months of the study to  $p < .001$  or less.

**Conclusions:** This study shows excellent efficacy and tolerability of frovatriptan as a pre-emptive medication for menstrual migraine and should be studied in double-blind manner.

**46. Title:** IV lidocaine—Effective treatment for refractory migraines and pain in the clinic

**Presenter:** John Claude Krusz, PhD, MD

**Biography:** Dr. Krusz has a multidisciplinary pain and headache management clinic in Dallas, Texas. He also has clinical interests in sleep, mood disorders, traumatic brain injury, and neuropsychiatric syndromes.

**Co-presenters:** Jane Cagle, LVN, IV Nurse, Anodyne Headache and PainCare; Stephanie Hall, MPH, Research Coordinator, Anodyne Headache and PainCare; Virginia Scott, BS, Research Coordinator, Anodyne Headache and PainCare

**Abstract:**

**Background:** Lidocaine has been used to treat neuropathic pain by virtue of its ability to block sodium channels, and thus block neuropathic pain signaling. On the theory that migraines or other headaches may be, in part, neuropathically mediated, we treated refractory migraines with this agent in a clinic setting.

**Objective:** To use IV lidocaine treatment for headache and pain flare-ups.

**Methods:** A total of 97 patients were treated (59 female/38 male; average age 40.8 yrs) for refractory migraine headaches and pain. 60 were treated for pain and 37 for migraines. Refractory pain disorders included: lumbar and cervical radiculopathy (n=42), TMD (n=5), anesthesia dolorosa (n=1), TN (n=4) and CRPS (n=8). A total of 147 IV treatments were administered. An initial dose of 3 mg/kg lidocaine was infused over 90 minutes. Patients rated initial migraine or pain severity (0 to 10 VAS) and at timed 15-minute intervals. Following initial treatment, additional 1.5 mg/kg to 2 mg/kg lidocaine was infused over 1 hour, if there were no side effects and if pain or migraine reduction was less than 50%.

**Results:** Pretreatment severity for migraines or pain (7.05/10) was reduced to 2.18/10 post-treatment ( $p < .001$ , 2 tailed t-test 12). 11 of 37 (32%) patients had complete abolishment of migraine. 15 patients were in status migrainosus. 19 of 60 (33%) patients had complete eradication of pain at the end of infusion. Average infusion time was 135 minutes, and average dose was 334 mg lidocaine. 50 patients were treated with a second dose of lidocaine. 6 patients experienced transient nausea or dizziness during infusion.

**Conclusions:** IV lidocaine can be used safely and with excellent success in the outpatient headache and pain clinic for the treatment of refractory pain and migraine flare-ups, but must be monitored closely during treatment. This study also raises questions about mechanisms of aberrant neurotransmitter activity involving sodium channels playing a role in refractory pain and migraine conditions. Double-blind studies are clearly warranted for this effective agent.

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**47. Title:** IV ketamine—Effective treatment for refractory migraines in the headache clinic

**Presenter:** John Claude Krusz, PhD, MD

**Biography:** Dr. Krusz has a multidisciplinary pain and headache management clinic in Dallas, Texas. He also has clinical interests in sleep, mood disorders, traumatic brain injury, and neuropsychiatric syndromes.

**Co-presenters:** Jane Cagle, LVN, IV Nurse, Anodyne Headache and PainCare; Stephanie Hall, MPH, Research Coordinator, Anodyne Headache and PainCare; Virginia Scott, BS, Research Coordinator, Anodyne Headache and PainCare

**Abstract:**

**Background:** We wanted to query whether migraine headaches may have similarity to neuropathic pain syndromes and if NMDA-glutamate receptor overactivity plays a role in the maintenance of refractory migraine headaches, at least after central sensitization takes place.

**Objective:** To study the efficacy and tolerability of IV ketamine for treating refractory migraines.

**Methods:** 48 patients (f=39, m=9) were treated for refractory migraines in the clinic. 13 had coexistent pain problems. 32 had allodynia. An IV was placed and pulse oximetry monitoring was used in each patient. 0.4 mg/kg ketamine was administered by IV infusion over 90 minutes. Patients rated their migraines on a 0 to 10 VAS. 14 patients received a second IV infusion (same or 10% greater dose). 9 patients received a third infusion using the same dosage strategy.

**Results:** Beginning migraine severity was 6.61/10, which was reduced to 3.4/10 after treatment ( $p < .001$ ; 2 tailed t test). Average ketamine infusion time was 145 minutes and the average dose of ketamine was 69 mg. All patients with allodynia had eradication of this symptom. Side effects were “spaciness” in 8 patients and a sense of exhilaration in 5 more, all transient. No person fell asleep during treatment.

**Conclusions:** IV ketamine for treating refractory migraines is a very effective form of treatment with an excellent safety margin. It speaks to the involvement of NMDA-glutamate receptors in the pathophysiology of refractory migraine and other headache and pain disorders. This agent should be studied in a double-blind, placebo-controlled manner.

**48. Title:** Intramuscular ketamine as treatment for refractory pain and headache in the outpatient clinic

**Presenter:** John Claude Krusz, PhD, MD

**Biography:** Dr. Krusz has a multidisciplinary pain and headache management clinic in Dallas, Texas. He also has clinical interests in sleep, mood disorders, traumatic brain injury, and neuropsychiatric syndromes.

**Co-presenters:** Jane Cagle, LVN, IV Nurse, Anodyne Headache and PainCare; Stephanie Hall, MPH, Research Coordinator, Anodyne Headache and PainCare; Virginia Scott, BS, Research Coordinator, Anodyne Headache and PainCare

**Abstract:**

**Background:** Ketamine is a potent blocker of NMDA-subtype

glutamate receptors, thought to play a role in pain transmission and migraine pathophysiology.

**Objective:** To study intramuscular (IM) ketamine in the clinic to treat pain flare-ups and refractory migraines where IV placement was technically difficult for the patient or where time was of the essence.

**Methods:** 9 patients (7=f, 2=m) were treated for refractory pain and headache in the clinic. A total of 19 IM injections of ketamine were given. 0.45mg/kg of ketamine was administered by IM injection [1/3 of this dose was given, 10 minutes apart] and the VAS headache or pain score rated. If there were no side effects, another 0.45 mg/kg was administered in the same fashion. Patients rated their pain/headache on a 0 to 10 VAS. 1 patient received 11 injections for recurring migraines using the same dosage schedule.

**Results:** Beginning pain severity (8.65/10) was reduced to 2.71/10 post-treatment ( $p < .001$ ). The average dose of ketamine was 68.3 mg. Side effects were “spaciness” in 3 patients and a sense of exhilaration in 1 patient. No person fell asleep during treatment.

**Conclusions:** IM ketamine for the treatment of refractory pain and migraine flare-ups is a very effective new form of treatment in the outpatient clinic. IM ketamine should be studied in a double-blind fashion.

## Neuropathic Pain

**49. Title:** A review of the epidemiology of painful diabetic peripheral neuropathy, postherpetic neuralgia, and less commonly studied neuropathic pain conditions

**Presenter:** Alesia Sadosky, PhD, MPH, MBA

**Biography:** Dr. Sadosky is Director of Global Outcomes Research at Pfizer, supporting one of their key pain products. Her interests are in health outcomes, clinical research, and public health.

**Co-presenters:** McDermott, SCM, ScD, Outcomes Research Consultant; Marcie E. Strauss, MPH; Nancy A. Brandenburg, PhD, Director of US Outcomes Research at Pfizer

**Abstract:**

**Background:** Although the burden of neuropathic pain (NeP) is well-recognized, the descriptive epidemiology of specific NeP conditions has not been well-described. While painful diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN) have been widely evaluated, many other peripheral and central NeP syndromes have been less frequently studied.

**Objective:** To summarize what is currently known regarding the prevalence of DPN, PHN, and other understudied NeP conditions for which there are fewer descriptive epidemiologic studies available.

**Methods:** Medline was searched using the terms “epidemiology,” “incidence,” and “prevalence,” in combination with appropriate terms identifying the syndrome or condition, to identify relevant articles with the most recent available epidemiologic data, through first half of 2006. Abstracts were reviewed to identify population-based studies or large case series in instances where no population-based studies were identified. English language articles were the primary source, but relevant population-based studies were translated from other languages.

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## Neuropathic Pain

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**Presenter:** Alesia Sadosky, PhD, MPH, MBA

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**Objective:** To summarize what is currently known regarding the prevalence of DPN, PHN, and other understudied NeP conditions for which there are fewer descriptive epidemiologic studies available.

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**Results:** Based on published global estimates, the prevalence of painful DPN in the diabetic population is 11% to 26%. In the general population, the prevalence of PHN and carpal tunnel syndrome is 7% to 27% and 2% to 16%, respectively; 23% to 58% of patients with multiple sclerosis and 10% to 80% of patients with spinal cord injuries were estimated to suffer from NeP associated with their conditions. The estimated prevalence of central post-stroke pain in stroke patients was 8% to 11%. There was inadequate data to summarize the prevalence of trigeminal neuralgia, glossopharyngeal neuralgia, and cervical radiculopathy.

**Conclusion:** The data suggest that while our knowledge is still incomplete, the high frequency of several of these conditions in specific populations should be considered an important impetus for further studies designed to evaluate their contribution to the overall burden of NeP.

**Disclosure:** This study was supported by Pfizer, Inc.

**50. Title:** Effectiveness of hyperbaric oxygen therapy for complex regional pain syndrome

**Presenter:** Allan M. Spiegel, MD

**Biography:** Dr. Spiegel completed his neurologic residency SUNY Down State and has been in solo practice, pharmaceutical clinical research, and hyperbaric oxygen therapy.

**Abstract:**

**Background:** Complex Regional Pain Syndrome (Reflex Sympathetic Dystrophy) is a debilitating neurological disorder usually precipitated by a trauma to a limb. The clinical manifestations include swelling of an extremity, severe hyperalgesic pain, changes in skin temperature and color, and weakness. Frequently, it is associated with trophic changes exemplified by loss of hair and abnormal nail growth.

**Objective:** To examine the ability of Hyperbaric Oxygen Therapy to reduce the symptoms commonly seen with this disorder in 5 consecutive patients.

**Methods:** 5 consecutive patients (1 male, 4 female) ages 24 to 66 with signs and symptoms of Complex Regional Pain Syndrome confirmed by an independent pain management specialist and disability present for 2 to 14 years despite aggressive medical management with stellate ganglion blocks, spinal stimulators, narcotic analgesics were referred for HBOT. Each patient received 20 to 30 treatments at 2.4 ATA for 90 minutes.

**Results:** All 5 patients had resolution of the hyperalgesic pain and swelling with return of normal limb sensation, temperature, color, strength and function; 2 of the 5 have returned to gainful employment.

**Conclusions:** Hyperbaric Oxygen Therapy reverses the reflex vasomotor disturbances thereby reducing swelling and enhancing oxygen perfusion of the effected tissues in patients with complex regional pain syndrome. HBOT should be considered a treatment option in patients with this disorder.

**51. Title:** Central sensitization, chronic pain syndromes, and pregabalin

**Presenter:** T. Kevin Murphy, PhD

**Biography:** Dr. Murphy is a Senior Clinical Director in Pfizer Pharmaceuticals' Global Medical organization, based in Pfizer's NY headquarters. He is a member of the team supporting Lyrica® (pregabalin).

**Co-presenters:** Jeannette A. Barrett, PhD, Pfizer Global Pharmaceuticals; Michael Tuchman, MD, Palm Beach Neurological Center

**Abstract:**

**Background:** Central sensitization, as first described by Woolf in 1983, appears to contribute to pathologic pain syndromes. Sustained activation of unmyelinated C-fibers at synaptic endings within the dorsal horn of the spinal cord may cause central sensitization. The release of glutamate and substance P by dense-core synaptic vesicles in C-fiber terminals appears to be required for central sensitization. The alpha2-delta ligands, gabapentin and pregabalin, reduce glutamate release (Maneuf et al, 2001) from hyperexcited neurons and decrease substance P release after spinal cord sensitization (Fehrenbacher et al 2003). Studies with healthy volunteers suggest that gabapentin (Dirks et al, 2002) and pregabalin (Chizh et al, 2007) can reduce central sensitization following pain-inducing stimuli.

**Objective:** To explore the involvement of central sensitization in chronic pain syndromes and the role of pregabalin in the treatment of chronic pain syndromes involving central sensitization.

**Methods:** Pregabalin has been studied in peripheral neuropathic pain syndromes, a central neuropathic pain syndrome, and fibromyalgia. We present pain relief data from these trials.

**Results:** Pregabalin consistently and significantly decreased pain from baseline in patients with peripheral neuropathic pain, central neuropathic pain, and fibromyalgia. Pregabalin showed efficacy as pain treatment in 9 of 11 peripheral neuropathic pain trials (painful diabetic peripheral neuropathy or postherpetic neuralgia), 1 of 1 central neuropathic pain trial (spinal cord injury), and 4 of 4 fibromyalgia trials. Significantly more pregabalin-treated patients experienced  $\geq 30\%$  and  $\geq 50\%$  pain reduction than those given placebo ( $p < 0.05$  to  $0.0001$ ). Mean Pain Score, assessed by patient daily diaries, showed significant pain relief typically by Week 1 with maintenance of pain control for duration of pregabalin treatment in patients across all indications.

**Conclusions:** These findings suggest that chronic pain syndromes share processes of central sensitization, and that pregabalin is likely to be efficacious in other chronic pain syndromes involving central sensitization.

**Disclosure:** This study was funded by Pfizer.

**Encore Presentation:** 2008 American Pain Society, May 9, 2008, Tampa FL

**52. Title:** Do mood symptoms affect response to pregabalin for neuropathic pain?

**Presenter:** T. Kevin Murphy, PhD

**Biography:** Dr. Murphy is a Senior Clinical Director in Pfizer

# POSTER ABSTRACTS

Pharmaceuticals' Global Medical organization, based in Pfizer's NY headquarters. He is a member of the team supporting Lyrica® (pregabalin).

**Co-presenter:** Birol Emir, PhD, Pfizer Global Pharmaceuticals

**Abstract:**

**Background:** Symptoms of anxiety and depression are commonly comorbidities of chronic pain syndromes, including painful diabetic peripheral neuropathy (DPN).

**Objective:** To investigate whether there were relationships between changes in pain and the severity of comorbid symptoms of anxiety and depression.

**Methods:** Data from 3 randomized, placebo (PBO)-controlled trials of pregabalin for the treatment of painful DPN were pooled and retrospectively analyzed. Patients received 300 mg/d pregabalin, 600 mg/d pregabalin, or PBO for 8 to 13 weeks. Endpoint-LOCF mean pain score (MPS) on a numeric scale of 0 (no pain) to 10 (worst possible pain) was the primary efficacy measure, and the Hospital Anxiety and Depression Scale anxiety (HADS-A) and depression (HADS-D) subscales were secondary efficacy measures. 663 patients received pregabalin; 367 received PBO.

**Results:** Baseline (BL) MPS was 6.5 for pregabalin and 6.3 for PBO patients; mean BL HADS-A score was 8.4 in both groups; mean BL HADS-D score was 7.3 in both groups. 27.8% and 30.7% of pregabalin and PBO patients had moderate-to-severe anxiety symptoms at BL (HADS-A  $\geq 11$  out of 21), and 22.0% and 20.3% of pregabalin and PBO patients had moderate-to-severe depression symptoms (HADS-D  $\geq 11$ ). Overall, treatment with pregabalin was associated with significant improvement in endpoint MPS vs. PBO (treatment difference, -0.36,  $p=.0168$ ). Examination of MPS by HADS-A and by HADS-D category showed significant improvement in MPS among patients with mild (BL score 8-10) or moderate-to-severe symptoms of anxiety or depression: mild anxiety, -0.42 ( $p=.0070$ ); mild depression, -0.48 ( $p=.0041$ ); moderate-to-severe anxiety, -0.71 ( $p=.0128$ ); moderate-to-severe depression, -0.83 ( $p=.0163$ ). The most common adverse events among pregabalin patients were dizziness (29% [vs. 6% PBO]) and somnolence (18% [vs. 5% PBO]). 14% of pregabalin and 6% of PBO patients discontinued because of AEs.

**Conclusions:** Pregabalin was associated with significant reductions in MPS, and pain relief appeared to be independent of BL anxiety and depression levels.

**Disclosure:** This study was funded by Pfizer.

## Diabetic Peripheral Neuropathy

**53. Title:** A survey of treatment practices in diabetic peripheral neuropathy

**Presenter:** Carl J. Possidente, PharmD, FASHP

**Biography:** Dr. Possidente is Medical Outcomes Specialist at Pfizer, Inc. He received his Doctor of Pharmacy degree from Albany College of Pharmacy, and has 21 years experience in hospital pharmacy practice.

**Co-presenter:** Rup Tandan, MD, FRCP, Professor and Vice Chairman of Neurology and Head of the Neuromuscular Disorders Section at the University of Vermont

**Abstract:**

**Background:** Diabetic peripheral neuropathy (DPN) is a common complication of diabetes. Approximately 11% to 26% of patients experience chronic pain impacting their quality of life.

**Objective:** To evaluate provider practices for identification and treatment of painful DPN.

**Methods:** A one-page written questionnaire was distributed to healthcare providers attending DPN educational programs conducted by a neurologist at New England locations in 2006.

**Results:** A total of 357 providers completed the questionnaire, representing an 80% response rate. The majority were primary care physicians. Nearly 70% of respondents lived in Vermont or Massachusetts, with the remainder equally distributed between Rhode Island, Connecticut, and New Hampshire. Providers noted that 76% of patients reported symptoms of DPN at  $\geq 50\%$  of visits. Almost all providers noted pain severity, affective symptoms, sleep disturbance, and impact on work and activities of daily living were important factors in their evaluation. Screening for DPN was considered to be important or extremely important by almost all providers; however, only 18% screened at every visit, and 16% rarely or never screened patients. The most commonly prescribed medications were anticonvulsants and tricyclic antidepressants. Although not recommended as first line of therapy for painful DPN, opioids were prescribed by 29% and NSAIDs by 31% of providers; 61% of providers instructed patients to titrate the dose of medications frequently or at every visit. Only 57% of providers used a quantitative pain scale to evaluate pain; 70% of providers assessed the effectiveness of medications at least frequently (75% of visits), and only 22% assessed effects at every visit.

**Conclusions:** Consensus guidelines recommend that once therapy is started, patients should be monitored and their pain evaluated at each visit. Our survey results reiterate the need for routinely questioning patients with DPN about pain, using pain scales, and employing medications proven to be effective in neuropathic pain.

**54. Title:** Long-term treatment of diabetic neuropathy with lacosamide

**Presenter:** Andrea Eggert, PharmD, BCPP

**Biography:** Dr. Eggert is the Clinical Science Manager at UCB, Inc. She received her Doctor of Pharmacy at the University of Texas at Austin and the University of Texas Health Science Center at San Antonio.

**Co-presenters:** Ronald Graf, MD, Principal Investigator at Cedar Research; Wendy Frye, BS, Associate Clinical Project Manager at Schwarz Biosciences, Inc.; Jeffrey Simpson, PhD, Clinical Trial Manager at Schwarz Biosciences, Inc.; Gary W. Jay MD, DAAPM, FAAPM, Medical Director, Pain, at Schwartz Biosciences, Inc.

**Abstract:**

**Background:** Lacosamide is a new antinociceptive and anticonvulsant drug under review by the FDA and EMEA for the treatment of painful distal diabetic neuropathy (DNP) and adjunctive therapy for partial onset seizures.

**Objective:** This ongoing, open-label study assessed the tolerability and safety of long-term lacosamide treatment in subjects with DNP, with the secondary objective of evaluating long-term efficacy.

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**Methods:** Subjects were enrolled from 2 double-blind and 1 open-label trials. Prior double-blind trial subjects completed a blinded transition phase and titration to an optimal lacosamide dose  $\leq$  600 mg/day. Prior open-label trial subjects could continue with their previous lacosamide dose or adjust to  $\leq$  600 mg/day. Dose adjustments were allowed throughout the trial. Adverse events (AEs), clinical assessments and withdrawal reasons were recorded. Efficacy measurements included an 11-point Likert scale pain evaluation and patient-rated impression of change (PGIC).

**Results:** At the time of this interim report, 242/451 subjects (53%) remained in the trial with 189 (42%) receiving treatment for  $\geq$  18 months. Most common reasons for early discontinuation included AEs (17%) and withdrawal of consent (13%). Most subjects (66%) utilized a lacosamide maintenance dose of 400 mg/day to 600 mg/day. The most frequently reported AEs ( $\geq$ 10%) were dizziness (21%), upper respiratory infection (14%), nausea (12%) and headache (10%). AEs leading to trial discontinuation ( $>$  1%) were dizziness (2.0%) and tremor (1.6%). Most AEs were mild or moderate in intensity. Of severe intensity-rated AEs, only dizziness (2%) occurred at a rate  $>$  1%. Mean change in Likert pain score from Baseline to the entire Maintenance phase was -3.82. Over 90% of subjects reported their pain as "better" on PGIC. Pain score reductions were sustained over the duration of the trial.

**Conclusions:** Lacosamide was generally well tolerated, and no serious safety concerns were identified with long-term treatment. The efficacy outcomes suggest that pain relief is sustained with long-term lacosamide treatment in subjects with DNP.

**Disclosure:** This study was supported by UCB.

**55. Title:** Trial results for lacosamide in painful diabetic neuropathy

**Presenter:** Aziz Shaibani, MD, FACP, FAAN

**Biography:** Dr. Shaibani is the Medical Director of the Nerve and Muscle Center of Texas. He received his MD from University of Mosul in Iraq.

**Co-presenters:** Patrick Kenney, Clinical Trial Manager at Schwarz Biosciences, Inc.; Jeffrey N. Simpson, PhD, Clinical Trial Manager at Schwarz Biosciences, Inc.; Sabine Bongardt, Clinical Program Director for Neuropathic Pain at Schwarz Biosciences GmbH

**Abstract:**

**Background:** Lacosamide (SPM 927, R-2-acetamido-N-benzyl-3-methoxypropionamide) is a functionalized amino acid that has shown activity in a wide range of animal models for pain and epilepsy.

**Objective:** To investigate the antinociceptive effects of lacosamide in diabetic neuropathic pain.

**Methods:** 469 patients were randomized (1:2:2:2) to placebo (n=66), 200 (n=141), 400 (n=125), or 600 mg/day (n=137) lacosamide treatment arms. Subjects titrated to their assigned dose then entered a 12-week maintenance phase. No dose adjustments were allowed. Subjects rated their pain twice daily using an 11-point Likert scale. Adverse events were assessed throughout the trial.

**Results:** Mean reduction in pain scores from baseline to the last 4 weeks of maintenance were -1.67, -2.01, -2.29, and -2.23 in the placebo, 200, 400, and 600 mg/day lacosamide arms, respectively,

and approached significance ( $p=.0507$ ) for the 400 mg/day lacosamide arm. A statistically significant separation between 400 and 600 mg/day lacosamide treatment and placebo arms was achieved early during titration and was also observed for the entire titration and maintenance period. Most AEs were mild or moderate in intensity and had their onset during the titration phase. The incidence rates of AEs were similar across all treatment arms. The rate of early discontinuations was 31.8%, 32.6%, 43.2%, and 66.4% in the placebo, 200, 400, and 600 mg/day lacosamide arms, respectively. The most frequently reported AEs were dizziness, nausea, balance disorder, tremor, and headache.

**Conclusions:** Lacosamide at doses of 400 mg/day and 600 mg/day significantly reduced pain scores in subjects with diabetic neuropathy during titration and the entire 12-week maintenance period of this trial. The 200 mg/day and 400 mg/day lacosamide doses were better tolerated than the 600 mg/day dose in this trial.

**Disclosure:** This study was supported by UCB.

**56. Title:** Evaluation of lacosamide in diabetic neuropathic pain trials

**Presenter:** Aziz Shaibani, MD, FACP, FAAN

**Biography:** Dr. Shaibani is the Medical Director of the Nerve and Muscle Center of Texas. He received his MD from University of Mosul in Iraq.

**Co-presenters:** Sabine Bongardt, Schwarz Biosciences GmbH; Kenneth Sommerville, MD, Vice President of Clinical Research at King Pharmaceuticals, Inc.

**Abstract:**

**Objective:** To evaluate the efficacy and safety of the investigational antinociceptive and anticonvulsant drug lacosamide dosed at 400 mg/day in the treatment of diabetic neuropathic pain.

**Methods:** Data were collected from Phase II and III double-blind, randomized, placebo-controlled trials. Three fixed-dose trials (SP742, SP743, SP768) contained a 12-week maintenance period; the Phase II flexible-dose trial (SP614) consisted of a 4-week maintenance period. Primary outcome was within-subject change in average daily pain score (11-point pain scale) from baseline to the last 4 weeks of maintenance for the fixed-dose trials and from baseline to the end of maintenance for the flexible-dose trial.

**Results:** Subjects receiving lacosamide 400 mg/day (n=426) showed numerically-reduced pain scores over placebo (n=291) in all trials. Results were statistically significant in two trials (SP614;  $p=.04$  SP742;  $p=.01$ ) and at the level of significance in SP768 ( $p=.0507$ ) for the primary variable. Significance was not reached in SP743, due to a strong placebo effect at the final visit. When using the secondary variable of change from baseline to the entire maintenance phase, lacosamide 400 mg/day significantly reduced pain over placebo in the fixed-dose trials ( $p=.02$ ,  $p=.01$  and  $p=.007$  for SP742, SP743 and SP768, respectively). Treatment with 400 mg/day lacosamide resulted in the occurrence of four adverse events with an incidence  $>$  5% and greater than placebo: dizziness (13.8%), fatigue (7.7%), nausea (6.8%), and tremor (5.6%).

**Conclusions:** Lacosamide 400 mg/day significantly reduced pain and showed good tolerability in clinical trials of diabetic neuropathic pain.

**Disclosure:** This study was supported by UCB.

**57. Title:** NGX-4010 in painful diabetic neuropathy

**Presenter:** Lynn R. Webster, MD, FACPM, FASAM

**Biography:** Dr. Webster is board certified in anesthesiology and pain management. His clinical research interests include pain and pain mechanisms, substance abuse and addiction, and the relationship between sleep and pain.

**Co-presenters:** Suzanne K. Gazda, MD, Integra Clinical Research, LLC; Jeffrey R. Medoff, MD, Medoff Medical, President and Medical Director of Vital Re:Search; Jeffrey Tobias, MD, Chief Medical Officer at NeurogesX, Inc., Gertruui F. Vanhove, MD, PhD, Senior Director of Clinical Development at NeurogesX, Inc.

**Abstract:**

**Objective:** To assess the efficacy and tolerability of NGX-4010, a high-concentration capsaicin dermal patch (capsaicin 8%), in patients with painful diabetic neuropathy (PDN) pretreated with 1 of 3 different topical anesthetics.

**Methods:** This randomized, open-label, multicenter 12-week trial included PDN patients with moderate-to-severe neuropathic pain in both feet (average Numeric Pain Rating Scale [NPRS] score of 3 to 8 inclusive). Patients received pretreatment with 1 of 3 topical anesthetics (LMX4<sup>®</sup>, Topicalaine<sup>®</sup>, or Betacaine<sup>®</sup>) followed by a single NGX-4010 treatment applied for 60 or 90 minutes. Efficacy was assessed by collection of daily NPRS scores for “average pain for the past 24 hours” and percent change in mean scores from Baseline to Weeks 2 to 12 were calculated. Safety and tolerability measures included continuous monitoring of adverse events (AEs) and periodic assessments of clinical laboratory parameters, vital signs, physical examination, electrocardiograms, dermal assessments, neurological/sensory assessments, and rescue pain medication usage. 91 PDN patients received treatment and were included in this analysis.

**Results:** Following treatment with NGX-4010, a mean decrease of 31% in NPRS scores from Baseline to Weeks 2 to 12 was observed; 47% of patients reported a 30% decrease and 34% reported a ≥ 50% decrease from Baseline in NPRS scores. The most common treatment-related AEs were application site burning and application site pain. AEs were generally mild or moderate in severity. No significant differences were observed between the 3 topical anesthetics with regard to tolerability or response to NGX-4010. Efficacy was similar for the 60- or 90-minute NGX-4010 treatments.

**Conclusions:** Treatment of PDN with NGX-4010 in conjunction with any of the 3 topical local anesthetics tested was generally well tolerated and demonstrated a reduction in pain over a 12-week period.

**Disclosure:** This study was sponsored by NeurogesX, Inc.

## Postherpetic Neuralgia

**58. Title:** One-hour application of NGX-4010 in postherpetic neuralgia

**Presenter:** Miroslav “Misha” Bačkonja, MD

**Biography:** Dr. Bačkonja is professor of Neurology, Anesthesiology, and Rehabilitation Medicine at the University of Wisconsin, where

his clinical and research interest is neuropathic pain, including pathophysiology, clinical assessment, and treatment.

**Co-presenters:** Edwin D. Duntzman, MD, Director and President of the Pain Treatment Facility of St. Louis and the A & A Pain Institute of St. Louis, Adjunct Clinical Assistant Professor at the University of Missouri School of Medicine; Gordon Irving, MD, Medical Director of the Swedish Pain and Headache Center at Swedish Medical Center in Seattle, Clinical Associate Professor in the Department of Anesthesiology at the University of Washington School of Medicine; E. Richard Blonsky, MD, Professor of Clinical Neurology at Northwestern University Medical School, Pain & Rehabilitation Clinic of Chicago; Gertruui F. Vanhove, MD, PhD, Senior Director of Clinical Development at NeurogesX, Inc.; Shiao-Ping Lu, MS, Director of Biometrics at NeurogesX, Inc.; Jeffrey Tobias, MD, Chief Medical Officer at NeurogesX, Inc.

**Abstract:**

**Background:** Current therapies for postherpetic neuralgia (PHN) rarely provide complete pain relief, and are often limited by side effects.

**Objective:** This study evaluated the efficacy and safety of a single 1-hour application of NGX-4010, a high-concentration capsaicin dermal patch (capsaicin, 8%), for the treatment of PHN.

**Methods:** This double-blind controlled study randomized 416 patients with PHN to NGX-4010 or a low-concentration control patch (capsaicin, 0.04%). After application of a topical local anesthetic, NGX-4010 or control was applied for 60 minutes to the painful area. Inclusion criteria included pain 6 months after herpes zoster lesion healing, and an average pain score of 3 to 9 on the 11-point Numeric Pain Rating Scale (NPRS). Following treatment, patients recorded their “average pain for the past 24 hours” NPRS score daily throughout the 12-week study period. Patient Global Impression of Change (PGIC) was assessed at Weeks 4, 8, and 12. The primary assessment was the percent reduction in NPRS from Baseline to Weeks 2 to 8.

**Results:** A single 1-hour application of NGX-4010 significantly reduced NPRS scores from Baseline to Weeks 2–8 compared with the control (mean change in NPRS score -32.0% vs. -24.4%;  $p=.011$ ). NGX-4010 reduced pain throughout the 12-week study period (Weeks 2 to 12, -32.3% vs. -25.0%;  $p=.017$ ). PGIC scores were improved in NGX-4010 recipients compared with controls at Weeks 4, 8, and 12.

**Conclusions:** Significantly more patients treated with NGX-4010 were rated as “much improved” or “very much improved” compared to the control at each time point ( $p<.05$  for all). Treatment was generally well tolerated; local, transient application site reactions were the primary adverse effect of treatment. This study demonstrates that a single 1-hour application of NGX-4010 is generally well tolerated and can significantly reduce pain for 12 weeks in patients with PHN.

**Disclosure:** This study was supported by NeurogesX, Inc.

**59. Title:** Dynamic allodynia in a trial of pregabalin in postherpetic neuralgia

**Presenter:** Jeannette A. Barrett, PhD

# POSTER ABSTRACTS

**Biography:** Dr. Barrett is Clinical Director with Pfizer Global Pharmaceuticals, New York, NY. She is involved in the development and execution of Phase IIIb/IV clinical development programs with pregabalin.

**Co-presenters:** Brett Stacey, MD, Oregon Health & Science University; Michael Rowbotham, MD, Pain Clinical Research Center at the University of California, San Francisco; Ed Whalen, PhD, Pfizer Global Pharmaceuticals; Kem Phillips, PhD, Pfizer Global Pharmaceuticals

**Abstract:**

**Background:** Despite its common occurrence in patients with PHN (> 50%), dynamic allodynia has not been routinely evaluated in large RCTs.

**Objective:** To evaluate the effect of pregabalin on Visual Analog Scale (VAS) ratings of dynamic (brush-evoked) allodynia in PHN in a placebo-controlled RCT.

**Methods:** The study consisted of a 7-day screening period, 28-day treatment phase, and 1-week taper. Patients (> 18 y) with PHN for 3 months, pain VAS score of 40 mm (100 mm scale), who completed the daily pain NRS > 4 times (average daily score 4; 0 to 10 scale) during 7-day screening. Time-to-onset of clinically meaningful pain relief was the primary efficacy measure, with VAS allodynia being a secondary measure and the focus of this analysis. A total of 91 patients were randomized to flexible-dosage pregabalin (optimized dose 150 mg/d to 600 mg/d BID); 88 to fixed-dosage 300 mg/d; and 90 to placebo for 4 weeks.

**Results:** Median time-to-onset of pain relief was 3.5 d, 1.5 d, and > 4 weeks for flexible, fixed, and placebo, respectively, and corresponded to meaningful pain relief achieved in 69.2%, 58.0%, and 30% of treatment groups, respectively. Fixed- and flexible-dosage pregabalin appeared superior to placebo as early as Days 1 and 2, respectively. Most patients (approximately 66%) had moderate-to-severe allodynia at baseline. Baseline-to-endpoint LS-mean changes in brush-evoked allodynia in PHN-affected areas for flexible-, fixed-dosage, and placebo groups were: -26.23 (p<0.0001) -20.81 (p=0.0075), and -11.83.

**Conclusions:** Endpoint improvement in allodynia correlated with improvement in pain for all groups. Improvements in mean weekly pain score and brush-evoked allodynia rating significantly correlated with improvement on PGIC. Both pregabalin regimens were well tolerated and associated with early onset and clinically meaningful, sustained pain relief and corresponding improvements in dynamic allodynia and PGIC scores in PHN patients.

**Disclosure:** This study was funded by Pfizer.

## Occupational Medicine

**60. Title:** Pain and work productivity in LBP patients taking HC/APAP CR

**Presenter:** Dave E. Webster, DO

**Biography:** Dr. Webster is a private-practice physician in Family Medicine and an investigator at Team Research of Central Texas, in Killeen, Texas.

**Co-presenters:** Darrell T. Herrington, DO, principal investigator of Benchmark Research, Associate Director of VistaCare Hospice, Board member of West Texas Medical Associates in San Angelo; Bruce C. Corser, MD, CPI, Medical Director at the Community Research and Sleep Management Institute, Cincinnati, Ohio, and Crestview Hills, Kentucky; Ronald Jay Rapoport, MD, FACR, Director of the Osteoporosis and Research Center at Charlton Memorial Hospital (CMH), rheumatologist at CMH/St. Anne's Hospital, Director of Phase III Clinical Research; Ara H. Dikranian, MD, rheumatologist at the San Diego Arthritis Medical Clinic; James W. Thomas, MS, Manager of Statistics at Abbott; Pamela G. Vo, MS, PharmD, Manager of Global Health Economics and Outcomes Research for Abbott; Steven E. Marx BS, MS, PharmD, RPh, Director of Global Health Economics & Outcomes Research (HEOR) in Global Pharmaceutical Research & Development at Abbott; Andrea Erickson Best, DO, MPH, is Global Project Head of Pain Research and Development at Abbott

**Abstract:**

**Objective:** To conduct a cost analysis of reduced work productivity (presenteeism) from a 56-week, open-label study in patients with moderate-to-severe chronic noncancer pain (ICD-9 code 719.49), and to calculate the potential economic effects of 12-hour extended-release hydrocodone 15 mg/acetaminophen 500 mg (HC/APAP CR) treatment.

**Methods:** As part of a larger clinical trial (1), the Work Productivity and Activity Impairment (WPAI) instrument was administered at baseline (n=252) and Weeks 24 and 56, to measure reduced productivity and overall work impairment due to health. The economic impact of improved work productivity and overall work impairment due to health after HC/APAP CR treatment was calculated as the difference in cost from baseline to Weeks 24 and 56. Analyses were also conducted by gender and pain intensity (0 to 10 numeric rating scale [NRS]).

**Results:** In low back pain (LBP) patients, impairment while working due to health decreased from baseline by 22%/18% at Week 24/56, for an average estimated cost-savings per employee of \$4738/\$8864 at Week 24/56. When the study population was stratified by gender, overall work impairment cost-savings to employers were estimated at \$4483/\$8478 at Week 24/56 for female employees and \$2959/\$7137 for male employees. When categorized by pain severity, both moderate (NRS 4-6) and severe (NRS 7-10) pain patients' productivity was improved with cost savings of \$1671/\$5370 (moderate) and \$4226/\$8529 (severe) at Week 24/56.

**Conclusions:** As assessed by the WPAI, this cost analysis demonstrated extended-release HC/APAP CR improved work productivity after 24 and 56 weeks of treatment in patients with LBP.

**Disclosure:** This study was supported by Abbott Laboratories.

**Reference:**

1. Webster D, Corser BC, Rapoport R, et al. Long-term efficacy and tolerability of a 12-hour, extended-release hydrocodone/acetaminophen: a 56-week, phase 3, open-label study. *Pain Med.* 2008;9(1):106-107.

**61. Title:** Impact of extended-release HC/APAP CR on work productivity in Osteoarthritis (OA)

**Presenter:** Darrell T. Herrington, DO

**Biography:** Dr. Herrington is principal investigator of Benchmark Research, Associate Director of VistaCare Hospice, and a Board member of West Texas Medical Associates, in San Angelo, Texas.

**Co-presenters:** Dave E. Webster, DO, private-practice physician in family medicine and an investigator at Team Research of Central Texas; Bruce C. Corser, MD, CPI, Medical Director at the Community Research and Sleep Management Institute in Cincinnati, Ohio, and Crestview Hills, Kentucky; Ronald Jay Rapoport, MD, FACR, Director of the Osteoporosis and Research Center at Charlton Memorial Hospital (CMH), rheumatologist at CMH/St. Anne's Hospital, Director of Phase III Clinical Research; Ara H. Dikranian, MD, rheumatologist at the San Diego Arthritis Medical Clinic; James W. Thomas, MS, Manager of Statistics for Abbott; Pamela G. Vo, MS, PharmD, Manager of Global Health Economics and Outcomes Research at Abbott; Steven E. Marx BS, MS, PharmD, RPh, Director of Global Health Economics & Outcomes Research (HEOR) in Global Pharmaceutical Research & Development at Abbott; Andrea Erickson Best, DO, MPH, Global Project Head of Pain Research and Development at Abbott

**Abstract:**

**Objective:** To conduct a cost analysis of work productivity from a 56-week open-label study in patients with moderate-to-severe noncancer pain (ICD-9 cod 719.49), and to calculate potential economic effects of treatment with 12-hour extended-release hydrocodone 15 mg/acetaminophen 500 mg (HC/APAP CR).

**Methods:** As part of a larger clinical trial (1), the Work Productivity and Activity Impairment (WPAI) instrument was administered at baseline (n=179) and Weeks 24 and 56 in patients with moderate-to-severe chronic pain. The economic impact of improved work productivity and overall work impairment due to health after HC/APAP CR treatment was calculated as the difference in cost from baseline to Week 24 and Week 56. Analyses by gender and pain intensity (0 to 10 numeric rating scale [NRS]) were also conducted.

**Results:** Among OA patients, impairment while working due to health decreased from baseline by 12% at Week 24 and 15% at Week 56. This translates to an average estimated cost savings per employee of \$2549/\$7434 at Weeks 24/56. When the study population was stratified by gender, overall work impairment cost savings were higher in females than in males by \$1524 at Week 24 and by \$1340 at Week 56. Categorized by baseline pain severity, severe pain patients (NRS 7-10) had higher cost-savings of \$2555/\$3159 at Weeks 24/56, compared to patients with moderate baseline pain (NRS 4-6).

**Conclusions:** This cost analysis, as assessed by the WPAI, demonstrates that 12-hour extended-release HC/APAP CR improved productivity while at work after 24 and 56 weeks of treatment in patients with OA.

**Disclosure:** This study was supported by Abbott Laboratories.

**Reference:**

1. Webster D, Corser BC, Rapoport R, et al. Long-term efficacy and tolerability of a 12-hour, extended-release hydrocodone/acetaminophen: a 56-week, phase 3, open-label study. *Pain Med.* 2008;9(1):106-107.

## Opioid Therapy and Management

**62. Title:** Predicting aberrant drug-related behavior among patients receiving opioids for pain management

**Presenter:** Todd M. Moore, PhD

**Biography:** Dr. Moore is an Assistant Professor in the Department of Psychology at the University of Tennessee. His research interests focus on the causes, correlates, and consequences of substance abuse.

**Co-presenters:** Ted Jones, PhD, clinical psychologist in private practice; Joe H. Browder MD, MBA, Director of Multidisciplinary Pain Program at Pain Consultants of East Tennessee; Susan Daffron, Senior Coordinating Nurse Practitioner at Pain Consultants of East Tennessee; Steven D. Passik, PhD, Associate Attending Psychologist in the Department of Psychiatry and Behavioral Sciences at Memorial Sloan-Kettering Cancer Center, Assistant Professor of Psychology in Psychiatry at Cornell University Medical College

**Abstract:**

**Background:** The ability to predict which patients are at risk for violating medication policies, known as aberrant drug-related behavior, is critical to a better understanding and reduction of such behaviors. Many pain management centers measure this risk using the Screener and Opioid Assessment for Patients with Pain (SOAPP), the Diagnosis, Intractability, Risk, and Efficacy inventory (DIRE), and/or the Opioid Risk Tool (ORT); however, little is known about how these measures compare to each other in predicting aberrant drug-related behavior.

**Objective:** To address how these measures compare to each other in predicting aberrant drug-related behavior among patients receiving opioids for pain management.

**Methods:** 48 patients, who attended a pain management center in Tennessee, but were later discharged for aberrant drug-related behavior, were evaluated. Study participants averaged 43.9 (SD=10.7) years of age and length in the program prior to discharge averaged 3.8 (SD=2.6) months. Patients referred for opioid medication for pain management participated in a semi-structured clinical interview with the staff psychologist, and completed the SOAPP, DIRE, and ORT. Patients returned to the pain management center monthly for medication management. We conducted analyses that compared the sensitivity (i.e., percentage of discharged patients who were rated as being "at risk" for aberrant drug-related behavior at baseline) of each self-report measure and the clinical interview in predicting discharge for aberrant drug-related behavior.

**Results:** Results showed the highest sensitivity for the clinical interview (.77) and the SOAPP (.72), followed by the ORT (.45) and the DIRE (.17). Combining the clinical interview with the SOAPP increased sensitivity to .90. Additional analyses will examine characteristics of individuals who were classified by these measures.

**Conclusions:** Results of the present study suggest that, among patients who were discharged for aberrant drug-related behaviors,

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the clinical interview and the SOAPP were most effective at predicting discharge at baseline. Implications for future research and clinical practice are discussed.

**63. Title:** Laxation response in methylnaltrexone-treated patients with opioid-induced constipation is independent of opioid dose level

**Presenter:** Robert Israel, MD

**Biography:** Dr. Israel is Senior Vice President of Medical Affairs at Progenics Pharmaceutical in Tarrytown, NY.

**Co-presenters:** Jay Thomas, MD, Associate Clinical Professor, Medicine Cancer Symptom Control Program at the University of California, San Diego, Moores Cancer Center; Neal Slatkin, MD, City of Hope National Medical Center in Duarte, California; Nancy Stambler, MS, Progenics Pharmaceutical; Russell Portenoy, MD, Chairman of the Department of Pain Medicine and Palliative Care at Beth Israel Medical Center, Professor of Neurology at the Albert Einstein College of Medicine

**Abstract:**

**Background:** Constipation is a distressing adverse effect of opioid therapy for treatment of moderate-to-severe pain. Methylnaltrexone is a selective mu-opioid receptor antagonist that blocks peripheral effects of opioids without effecting analgesia.

**Objective:** To evaluate whether laxation response was influenced by opioid dosage.

**Methods:** A double-blind study in patients (n=154) with opioid-induced constipation and advanced illness taking opioids for  $\geq 2$  weeks demonstrated that methylnaltrexone induced laxation within 4 hours after a single dose of 0.15 or 0.30 mg/kg in 61.7% and 58.2% of patients, respectively, compared with 13.5% of those receiving placebo ( $p < 0.0001$ ). A secondary analysis was performed to compare the percentage of patients achieving laxation within 4 hours of methylnaltrexone dosing among patients receiving low ( $< 80$  mg/d), medium (80 to  $< 200$  mg/d), or high ( $\geq 200$  mg/d) opioid dosage. For this analysis, the baseline opioid dosage was converted into oral morphine equivalents (mg) using a standard conversion table. Opioid dosage and laxation response to methylnaltrexone were evaluated in a logistic regression model and tested using Wald chi-square.

**Results:** There was no significant relationship between opioid dosage and laxation response within 4 hours. After methylnaltrexone 0.15 mg/kg, laxation occurred in 83.3%, 45.5%, and 58.3% of patients receiving low, medium, and high doses of opioids, respectively (n=12, 11, and 24, respectively). After administration of methylnaltrexone 0.30 mg/kg, laxation occurred in 30.8%, 61.1%, and 70.8%, respectively (n=13, 18, and 24, respectively). For either dosage of methylnaltrexone, response rates were significantly greater for methylnaltrexone than placebo at all opioid dose levels ( $p < 0.0001$ ).

**Conclusions:** In a post-hoc analysis of this study, laxation response after a single methylnaltrexone dose did not correlate with baseline opioid dosage. This finding suggests the viability of fixed initial dosing irrespective of opioid dose level.

**64. Title:** Hospice survey on pain management, drug abuse, and diversion

**Presenter:** Kenneth L. Kirsh, PhD

**Biography:** Dr. Kirsh is a clinical psychologist at The Pain Treatment Center of the Bluegrass as well as an assistant professor at the University of Kentucky College of Pharmacy.

**Abstract:**

**Background:** Pain management is an essential aspect of the palliative care of the dying patient. For most patients receiving hospice care, pain management proceeds in an uneventful fashion where issues of drug addiction or diversion are concerned. However, when patients or their family members have pre-existing substance use problems, management becomes more difficult and complex. Hospice staff struggle disproportionately with this small percentage of patients and must be attentive to signs indicating problems with substance abuse or drug diversion in their cases and develop case management strategies for coping with these challenges.

**Methods:** We conducted an NIH-funded (5R21NR009916-02) needs-based assessment of frontline care workers (ie, nurses, Certified Nursing Assistants, chaplains, social workers) on the topic of pain management for the purpose of identifying barriers to effective treatment and to explore their perceptions about the prevalence of prescription drug abuse, theft, and diversion from the homes of dying patients. The needs assessment was conducted through focus groups, key informant interviews, and assessment of frontline care workers (n=340) at Hospice of the Bluegrass in Kentucky.

**Results:** Findings will be presented along with the ramifications of the data for nationwide palliative pain efforts. The data will shed light on a) the current knowledge base and new findings regarding pain management and addiction issues in hospice and palliative care efforts, and b) the impact of self-efficacy and job satisfaction on the belief system of frontline care workers regarding pain management and issues of drug abuse and diversion.

**65. Title:** Development of a chemical coping tool for pain management

**Presenter:** Kenneth L. Kirsh, PhD

**Biography:** Dr. Kirsh is a clinical psychologist at The Pain Treatment Center of the Bluegrass as well as an assistant professor at the University of Kentucky College of Pharmacy.

**Co-presenter:** Steven D. Passik, PhD, Associate Attending Psychologist at Memorial Sloan Kettering Cancer Center in New York City and Associate Professor of Psychology at the Weill Medical College of Cornell University

**Abstract:**

**Background:** There is a large group of patients between the extremes of complete medication compliance and frank addiction; those who display aberrant behaviors periodically, who may have a mixed response to opioid therapy, the overall results of which are less than satisfying (often in the domain of functionality) to the clinician. We have used the term chemical coping to describe this vast middle ground and seek to begin a line of research starting with the

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development of a clinically useful tool to identify this subset of patients.

**Methods:** In the current study, a total of 100 patients completed the Chemical Coping Inventory (CCI). The average age of the sample was 44.41 years (SD=10.42, range=19 to 65) and was comprised of 61 women and 39 men.

**Results:** Scores on the CCI ranged from 45 to 93 (mean=68.21, SD=11.12), although this response only accounts for 42% of the possible range (38 to 152) of the original instrument. The CCI also exhibited adequate initial internal consistency as measured by a Cronbach's alpha of 0.84. The 38 items were examined from multiple approaches and ultimately reduced to 29 items. Total scale internal consistency yielded a coefficient alpha of 0.84. The mean of the revised scale was 53.22 (SD=9.55). An intraclass correlation coefficient was also conducted, which revealed good overall cohesion (ICC=.15,  $F_{99,2772}=6.20$ ,  $p<.0001$ ). Reliability of the 4 individual subscales also was examined. Alphas ranged from 0.27 to 0.83.

**Conclusions:** The middle ground between compliant medication use and addiction which we call "chemical coping" is poorly understood and woefully under-researched. Despite this gap in our knowledge base, it is an often observed phenomenon. The further refinement of our tool to identify these characteristics can lead to better treatment outcomes and earlier interventions to help improve compliance with medication regimens.

**66. Title:** Cigarette smoking predicts aberrant drug-taking behavior in opioid therapy for persistent pain: A qualitative systematic review

**Presenter:** Lara Dhingra, PhD

**Biography:** Dr. Dhingra is an attending psychologist in the Department of Pain Medicine and Palliative Care at Beth Israel Medical Center, and assistant professor in the Departments of Neurology and Psychiatry and Behavioral Sciences at the Albert Einstein College of Medicine.

**Co-presenter:** Steven D. Passik, PhD, Associate Attending Psychologist at Memorial Sloan Kettering Cancer Center in New York City and Associate Professor of Psychology at the Weill Medical College of Cornell University

**Abstract:**

**Background:** Smoking rates among adults with persistent pain are high (30% to 64%) compared to the general population (21%). Furthermore, current evidence indicates that pain patients who smoke are at higher risk for aberrant drug-taking behavior (ADTB) on opioid therapy compared to nonsmokers. Aberrant drug-taking behaviors involve a spectrum of nonadherent behaviors with opioid use that predict addiction-related outcomes.

**Objective:** The goal of this review was to qualitatively examine studies on smoking and ADTB in subjects with persistent pain. Method: A systematic literature search was conducted using PubMed, PsychInfo, and Medline with the four concepts: smoking, pain, aberrant behaviors, and opioids. A search for each concept was conducted separately and then combined.

**Results:** Six studies showed that current smoking is associated with higher levels of analgesic use, more ADTB, and greater likelihood of substance abuse than nonsmoking. Michna and colleagues (2004)

showed that current smoking and an index of tobacco dependence (eg, smokes within 1 hour of waking) were among the most useful predictors of problems with opioid use among patients. In this study, 82% of patients at high-risk for ADTB were smokers. Of note, two screening instruments that assess risk potential for nonadherence with opioid use include smoking in determining risk: the Screening Instrument for Substance Abuse and the Screener and Opioid Assessment for Patients in Pain. Most studies were retrospective and did not offer an explanation of the association.

**Conclusions:** This systematic review showed that pain patients who smoke are at higher risk for ADTB on opioid therapy compared to nonsmokers. Despite these findings, smoking is a poorly understood risk factor for ADTB. No studies have suggested guidelines for opioid therapy among pain patients who continue to smoke. Clinical pain management would be aided by an evidence-based approach for treatment that addresses different risk profiles for abuse.

**67. Title:** Alcohol does not compromise abuse-resistant CR oxycodone

**Presenter:** Annelies de Kater, PhD

**Biography:** Dr. de Kater is Senior Director of Preclinical Development at Pain Therapeutics, Inc. in San Mateo, California.

**Co-presenters:** Peter Butera, Vice President of Clinical Operations at Pain Therapeutics, Inc.; J. Eric Haux, PhD, Senior Scientist at Pain Therapeutics, Inc.; Grant L. Schoenhard, PhD, Chief Scientific Officer, Pain Therapeutics, Inc.; Nadav Friedmann, PhD, MD, Chief Operating Officer at Pain Therapeutics, Inc.

**Abstract:**

**Background:** Abuse of controlled-release (CR) oxycodone remains a serious health concern. Abusers commonly defeat the controlled-release mechanisms by dissolving oxycodone tablets in alcohol. Ingesting the alcohol-dissolved tablet results in 'dose-dumping' and a quick, powerful euphoric high that can be fatal or lead to opioid addiction. The development of abuse-resistant opioid medications is a major, however elusive, public health goal.

**Objective:** The present study was conducted in healthy volunteers to demonstrate the effects of alcohol on Remoxy™, a unique formulation of CR oxycodone specifically designed to resist common methods of abuse.

**Methods:** This single-center, randomized, 4-way crossover study evaluated the rate and extent of absorption of oxycodone from Remoxy™, when taken with water or ethanol. After signing informed consent, 37 subjects were fed and pretreated with the opioid antagonist naltrexone (to minimize opioid-related adverse events). In each treatment session, subjects ingested a single Remoxy™ 40 mg capsule while drinking 240 mL of either water alone, 4% ethanol, 20% ethanol, or 40% ethanol. Ethanol quantities were designed to simulate the amount of alcohol consumed in a "binge drinking" session.

**Results:** The oxycodone C<sub>max</sub> after ingesting Remoxy was 45.3 ng/mL with water alone, versus 45.0, 39.0, and 49.7 ng/mL, with 4%, 20% and 40% ethanol, respectively. The shape of the plasma concentration time curve was not affected by ethanol. There was no

effect on total exposure; the ratios for AUC<sub>inf</sub> of water co-ingestion to ethanol co-ingestion were 1.00, 1.06, and 1.14, with respective increasing concentrations of ethanol.

**Conclusions:** Remoxy™ is highly resistant to dissolution in alcohol, and consuming Remoxy™ with up to 40% ethanol did not defeat its controlled-release formulation. This prevention of ‘dose-dumping’ presumably prevents the quick, powerful euphoric high sought by recreational drug abusers, and also safeguards against patient co-ingestion of alcohol. These data suggest that Remoxy™ represents a safer alternative to current CR oxycodone.

**Disclosure:** This study was supported by Pain Therapeutics, Inc. and King Pharmaceuticals, Inc.

**68. Title:** Abuse-resistant, controlled-release oxycodone treats chronic pain

**Presenter:** Tim Merrigan, MD

**Biography:** Dr. Merrigan is the Associate Director of Clinical Development at Pain Therapeutics, Inc. in San Mateo, California.

**Co-presenters:** Nadav Friedman, PhD, MD, Chief Operating Officer at Pain Therapeutics, Inc.; Peter Butera, Vice President, Clinical Operations at Pain Therapeutics, Inc.; Vicki Klutzaritz, Associate Director, Clinical Data Management at Pain Therapeutics, Inc.; Debra Gilmore, RN, Associate Director, Clinical Operations at Pain Therapeutics, Inc.; Lynn Webster, MD, FACPM, FASAM, Medical Director Lifetree Clinical Research and Pain Clinic in Salt Lake City.

**Abstract:**

**Background:** Abuse and diversion of controlled-release (CR) oxycodone is a serious health concern. Abusers easily defeat the controlled-release mechanism by crushing or dissolving a tablet. Ingesting a fractioned tablet produces ‘dose-dumping’, this results in a quick, powerful euphoric high that can be fatal or lead to opioid addiction. Thus, the development of abuse-resistant opioid medications remains a major, but elusive, public health goal.

**Objective:** A Phase III study was conducted to test the safety and analgesic efficacy of Remoxy™, a unique formulation of CR oxycodone specifically designed to resist common methods of abuse, such as crushing, snorting, heating, freezing, dissolution in alcohol.

**Methods:** After signing informed consent, meeting screening criteria, and completing a titration period, 412 patients with moderate-to-severe pain due to osteoarthritis (OA) of the hip or knee were randomized to Remoxy™ BID or placebo over a 12-week treatment period. During weeks 1 to 4, patients were allowed to titrate their total daily dose of study medication (range: 10 mg to 80 mg). After week 4, the dose was fixed.

**Results:** Patients on Remoxy™ reported significantly lower pain intensity scores over the 12-week treatment period, as evidenced by the primary endpoint, area under the curve for change in pain intensity (p=0.007). Patients on Remoxy™ also reported significantly better scores on Global Assessment (p=0.007), Quality of Analgesia (p=0.004), pain subscales of the WOMAC™ Osteoarthritis Index (p=0.023), and other secondary endpoints. Adverse events were limited to common and expected opioid-related side-effects. Dropout rates were 36% for placebo and 34% for Remoxy™.

**Conclusions:** This is the first large, well-controlled clinical study demonstrating analgesic efficacy of an abuse-resistant, CR formulation of oxycodone. Surprisingly, we believe this is also the first study to ever demonstrate the analgesic efficacy of any twice-daily formulation of oxycodone over 12-weeks in patients with chronic pain.

**Disclosure:** This study was supported by Pain Therapeutics, Inc. and King Pharmaceuticals, Inc.

**69. Title:** Extended-release oxymorphone for opioid-failure, intractable pain patients

**Presenter:** Forest Tennant MD, Dr PH

**Biography:** Dr. Tennant is the Director of the Veract Intractable Pain Clinic in West Covina, California, and Editor Emeritus of Practical Pain Management.

**Abstract:**

**Background:** Oxymorphone is the newest oral opioid to become available for treatment of severe pain. It has some unique metabolic characteristics in that it is the end metabolite of morphine-oxycodone metabolism, and minimally-activated liver enzymes. Oxymorphone has great lipid solubility and opioid receptor binding affinity. The long-acting commercial formulation maintains a therapeutic serum concentration for about 12 hours.

**Objective:** To determine if extended-release oxymorphone proves helpful in managing opioid-failure, severe-pain patients.

**Methods:** 20 intractable pain patients who were treated with high dosages of a long-acting opioid (fentanyl, oxycodone, morphine, or methadone), plus one of more short-acting opioids (hydrocodone, hydromorphone, morphine, oxycodone), were selected for study. They were selected because they, and family members, declared their opioid regimen failed to provide adequate pain control for consistent mental and physical functions. Poor pain control was validated by failure to control excess sympathetic discharge signs and symptoms including pulse rate, blood pressure, skin temperature, and serum adrenal hormone levels. Extended-release oxymorphone was initiated at a dosage of 10 mg every 12 hours and titrated upward until the patient achieved adequate, self-reported pain control and stable sympathetic discharge symptoms.

**Results:** 6 patients did not tolerate oxymorphone due to nausea, dizziness, anxiety or dysphoria and ceased treatment. The remaining 14 patients achieved enhanced pain control as evidenced by self-report and normalization of pulse rate, and blood pressure. End-point oxymorphone dosage ranged from 40 mg to 600 mg per day. All 14 patients who remained on oxymorphone lowered dosages of one or more other opioids, but did not totally cease any opioid.

**Conclusions:** The addition of extended-release oxymorphone was a therapeutic, positive addition to an opioid-regimen that failed to provide adequate pain control.

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**70. Title:** Methadone deaths poorly correlate with serum concentrations

**Presenter:** Forest Tennant MD, Dr PH

**Biography:** Dr. Tennant is the Director of the Veract Intractable Pain Clinic in West Covina, California, and Editor Emeritus of Practical Pain Management.

**Abstract:**

**Background:** There has been a recent upsurge of sudden deaths among pain patients prescribed methadone. The usual explanation for death by coroners who find methadone in blood at autopsy is “methadone overdose or toxicity.” The toxic effect is most commonly believed to occur due to induction of cardiac conduction dysfunction.

**Objective:** To determine if dosage and/or chronicity may contribute to sudden death in long-term methadone patient.

**Methods:** Reported here are 32 severe, chronic pain patients who have taken methadone daily for over 4 months, and who are not clinically impaired in that they do not appear sedated, ambulate normally, carry-on activities of daily living, and the majority drive a car or work. Their daily methadone dosages range from 40 mg to 600 mg, and their serum concentrations range from 60 ng/ml to 2580 ng/ml.

**Results:** There was essentially no correlation between daily dosage, serum concentration, or longevity of administration.

**Conclusions:** These data question the premises that daily methadone dosage, blood level, and toxicity are necessarily related. Since these patients have taken methadone over an extended period, any cardiac conduction defect would likely have already occurred. When death occurs in a pain patient who takes methadone, the cause must not be simply assumed to be an overdose or toxic reaction of methadone.

## Oral Pain

**71. Title:** 670 nm HEALS® photobiomodulation for ulcerative mucositis

**Presenter:** Janis T. Eells, PhD

**Biography:** Dr. Eells is currently the Wisconsin Distinguished Professor in Department of Health Sciences at the University of Wisconsin, Milwaukee.

**Co-presenters:** David Margolis, MD, Associate Professor of Pediatrics, Medical College of Wisconsin, Milwaukee; Brian D. Hodgson, DDS, Assistant Professor, School of Dentistry, Marquette University; Harry T. Whelan, MD, Bleser Professor of Neurology, Medical College of Wisconsin, Milwaukee

**Abstract:**

**Background:** Ulcerative oral mucositis (UOM) is a common and debilitating side effect of radiation therapy and chemotherapy that leads to increased morbidity. Far-red to near-infrared light therapy has been shown to improve wound healing in experimental and clinical studies.

**Objective:** The purpose of this study was to test the hypothesis that 670 nm HEALS® light emitting diode (LED) treatment would protect against the development of ulcerative oral mucositis in pediatric bone marrow transplant (BMT) recipients.

**Methods:** 32 consecutive pediatric patients undergoing myeloablative therapy were treated with 670 nm LED once per day for 14 days post BMT at an energy density of 4 J/cm<sup>2</sup>. Patients received 670 nm LED treatment on the left extraoral epithelium and sham treatment on the right. Subsequent to the light treatment, patients were asked to rate left and right buccal pain as compared to throat pain, which served as an untreated control.

**Results:** 670 nm-LED treatment produced a significant reduction in left and right buccal pain (48% and 39% respectively) when compared to throat pain. In addition, the incidence of UOM in this patient population was decreased, with only 53% of patients developing UOM, compared to historical epidemiological data, indicating that 70-90% of the patient population receiving BMT would have developed UOM.

**Conclusions:** The results of this clinical trial demonstrate that 670 nm-LED treatment is an effective preventive countermeasure to the development of oral mucositis in cancer patients. A multi-centered, double-blind trial of 670 nm LED treatment for oral mucositis is currently underway at the Medical College of Wisconsin and the University of Alabama-Birmingham.

**Disclosure:** Supported by DARPA N66001-01-8969; NASA SBIR NAS8-99015 and NAS8-97277; the Bleser Endowed Professorship and Quantum Devices, Inc.

**72. Title:** Diclofenac soft gelatin capsule for postsurgical dental pain

**Presenter:** John R. Zuniga, DMD, MS, PhD

**Biography:** Dr. Zuniga received his DMD from Tufts University, a certificate in OMFS and PhD in Neuroscience from the University of Rochester, and is chair of OMFS at the University of Texas, Southwestern.

**Co-presenters:** Hans Malmström, DDS, Eastman Dental Center at the University of Rochester; Boyd J. Tomasetti, DMD, Rocky Mountain Oral & Maxillofacial Surgery, School of Dentistry at the University of Colorado; Stephen Boesing, MS, Xanodyne Pharmaceuticals, Inc.

**Abstract:**

**Background:** Diclofenac potassium for the treatment of acute pain may be limited by inconsistent absorption characteristics, which could lead to delayed and/or inconsistent analgesia. Diclofenac potassium soft gelatin capsule (DPSGC) is a formulation using patented ProSorb® technology, designed to facilitate rapid and consistent absorption compared with immediate-release diclofenac potassium tablets and may decrease time to analgesic onset.

**Objective:** To assess the safety and efficacy of DPSGC in adult patients (n=249) with pain following third molar extraction, through the use of a multicenter, randomized, parallel-group, double blind, placebo-controlled phase 3 study.

**Methods:** Patients experiencing a requisite level of pain (at least 50 mm out of 100 mm on a visual analog scale (VAS) within 4 hours after surgery) were randomized to receive single doses of DPSGC 25 mg, 50 mg, 100 mg, or placebo. Pain intensity and relief were assessed for 6 hours following dosing. The primary efficacy endpoint was summed pain intensity difference over 6 hours (SPID6). Other endpoints included SPID3 and total pain relief at 3 and 6 hours

(TOTPAR3 and TOTPAR6). Median times to onset of perceptible and meaningful pain relief were assessed using the two stopwatch method. Safety and tolerability were evaluated for 6 hours following dosing.

**Results:** SPID and TOTPAR scores at 3 and 6 hours were significantly improved for patients in all DPSGC groups compared with placebo ( $p<.0001$ ). The median times to onset of perceptible and meaningful relief were significantly shorter in all DPSGC groups compared with placebo, including the DPSGC 25 mg group (25 min,  $p=.0002$ , and 52 min,  $p<.0001$ , for perceptible and meaningful relief, respectively). DPSGC was well tolerated with no serious adverse events observed.

**Conclusions:** These data show DPSGC was safe and efficacious in patients requiring fast pain relief following dental surgery (third molar extraction).

**Disclosure:** This study was supported by Xanodyne Pharmaceuticals, Inc.

## Osteoarthritis

**73. Title:** Tanezumab, an anti-NGF monoclonal antibody, for treatment of pain due to osteoarthritis

**Presenter:** Thomas J. Schnitzer, MD, PhD

**Biography:** Dr. Schnitzer's research interests focus on the development and evaluation of new therapeutics for the treatment of osteoarthritis, osteoporosis, and pain, through clinical trials in phases I-IV.

**Co-presenters:** Nancy E. Lane, MD, Distinguished Professor of Medicine, Division of Rheumatology, Director of the Center for Healthy Aging, and Vice Chair for Research, Department of Medicine at University of California, Davis; Michael D. Smith, PhD, Director of Clinical Statistics, Pfizer Global Research & Development; Mark T. Brown, MD, Executive Director, Global Clinical Lead, Clinical Research & Development at Pain Therapeutics, Pfizer Inc.

**Abstract:**

**Background:** Increased expression of nerve growth factor in injured and inflamed tissue is associated with pain.

**Objective:** To investigate whether tanezumab, a humanized monoclonal antibody that specifically binds nerve growth factor, may relieve chronic joint pain in osteoarthritis of the knee.

**Methods:** This 16-week, randomized, double-blind, placebo-controlled, dose-ranging study (NCT00394563) evaluated tanezumab, administered intravenously on Day 1 and Day 56 in 450 men and women, aged 40 to 78 years of age, with moderate-to-severe knee pain due to osteoarthritis, who had failed non-opiates. The primary efficacy measures were walking knee pain (determined on a 100 mm VAS scale, assessed daily) and subject global assessment (SGA) of response to therapy. Adverse events (AEs) were also assessed.

**Results:** All treatment groups showed significant improvement compared with placebo in primary endpoints. Mean walking pain scores at baseline ranged from 68.1 to 72.4 across all groups; the mean change from baseline over the treatment period (Weeks 1 to 16) was -16.0 for placebo and, from lowest to highest dose, was -33.0, -36.9, -31.8, -44.0, and -43.8, respectively, in the tanezumab groups. Mean differences from placebo ranged from -15.8 to -28.0

(each dose  $p<0.001$ ). Improvement in SGA was noted over Weeks 1 to 16 in all tanezumab groups (each dose  $p<0.005$  vs. placebo). The incidence of any AE was 55% with placebo and 68% across the tanezumab groups. Across the tanezumab groups, the most common AEs were headache (8.9%), upper respiratory tract infection (7.3%), and paraesthesia (6.8%).

**Conclusions:** Patients with knee osteoarthritis showed greater improvements in pain and SGA with tanezumab compared with placebo, with greater pain reduction obtained with the higher doses. Tanezumab was well-tolerated in this study.

**Disclosure:** This study was supported by Pfizer, Inc.

**74. Title:** Duloxetine 60 to 120 mg versus placebo in the treatment of patients with osteoarthritis (OA) knee pain

**Presenter:** Ellen Schoenberger

**Biography:** Ms. Schoenberger is a Neuroscience Medical Liaison with Eli Lilly. Ellen received her B.S. in Pharmacy from University of Illinois, and was with The Upjohn Company in various medical and marketing positions before joining Eli Lilly.

**Co-presenters:** Amy S. Chappell, MD, Clinical Research Physician at Eli Lilly; Melissa J. Ossanna, PhD, Communication Consultant at Eli Lilly; Hong Liu-Seifert, PhD, Research Scientist at Eli Lilly; Jerry Hall, MD, Clinical Research Physician; Harry Collins, MD, Physician of Family and Geriatric Medicine at Anderson & Collins Clinical Research, Inc.

**Abstract:**

**Objective:** To assess efficacy of duloxetine (DLX) 60-120 mg once daily compared to placebo (PBO) on treatment of OA knee pain.

**Methods:** This was a 13-week, randomized, double-blind, parallel, placebo-controlled trial meeting American College of Rheumatology clinical and radiographic criteria for OA of the knee, with pain for  $\geq 14$  days of each month for 3 months and mean 24-hour average pain of  $\geq 4$  on a scale of 0 (no pain) to 10 (worst pain possible). Patients with major depressive disorder were excluded. Patients were randomized to DLX 60 mg once daily ( $n=111$ ) or PBO ( $n=120$ ) and stratified by non-steroidal anti-inflammatory (NSAID) use. At week 7, those receiving active treatment were re-randomized to DLX 60 mg or 120 mg to assess differences between doses. The primary efficacy variable was reduction of pain severity measured by weekly mean of the 24-hour average pain scores. Secondary measures: Patient Global Impressions of Improvement (PGI-I), Western Ontario and McMaster Universities (WOMAC) pain and physical functioning subscales, Clinical Global Impressions of Severity (CGI-S), and Brief Pain Inventory (BPI)-Severity.

**Results:** DLX was superior to PBO on mean 24-hour average pain reduction from baseline ( $p<0.001$ ) separating from PBO at Week 1 and throughout treatment ( $p\leq 0.05$ ). Compared to PBO, DLX treatment resulted in greater reduction in WOMAC scores for pain (DLX -4.64, PBO -3.24,  $p=0.003$ ) and physical functioning (DLX -16.36, PBO -11.18,  $p=0.001$ ), greater reductions in BPI average pain severity ( $p<0.001$ ), and greater improvement on patient (PGI-I  $p=0.002$ ) and clinician (CGI-S  $p=0.001$ ) global assessments. Efficacy was seen regardless of NSAID strata. Discontinuations due to adverse events (DLX 13.5%, PBO 5.8%), and lack of efficacy (DLX

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1.8%, PBO 2.5%), and rates of treatment-emergent adverse events did not differ significantly between treatment groups.

**Conclusions:** Duloxetine 60-120 mg once daily was effective in reduction of pain and improvement in function in patients with OA knee pain.

**Disclosure:** This study was supported by Eli Lilly and Company.

**75. Title:** Efficacy of morphine sulfate ER with sequestered naltrexone

**Presenter:** James B. Jones, PharmD, MD

**Biography:** Dr. Jones has industry experience in analgesia with COX-2 inhibitors and is currently Vice President of Clinical Development at Alharma Pharmaceuticals.

**Co-presenters:** Martin E. Hale, MD, Assistant Professor of Neurology at Nova South Eastern University, and research affiliation with Gold Coast Research; George Wagner, BS, Alharma Pharmaceuticals; David D. Morris, PhD, Director of Statistics at WebbWrites, LLC, and Associate Professor of Statistics at Northern Illinois University; Joseph W. Stauffer, DO, Adjunct Assistant Professor at Johns Hopkins University Hospital and Chief Medical Officer and Senior Vice President of Clinical Research & Medical Affairs at Alharma Pharmaceuticals

**Abstract:**

**Background:** ALO-01 (Embeda™) (morphine sulfate extended-release with sequestered naltrexone hydrochloride) Capsules, an investigational drug intended for chronic, moderate-to-severe pain, contains sequestered naltrexone, intended for release only upon product tampering (crushing, chewing) to mitigate opioid-induced euphoria.

**Methods:** This multicenter, randomized, double-blind, placebo-controlled study compared efficacy of ALO-01 vs. placebo. Patients were adults ( $\geq 21$  years) with primary diagnosis of osteoarthritis of hip or knee (ACR criteria) (1,2) and target joint pain within the last 90 d, not consistently relieved with non-opioids or tramadol, or requiring oral morphine equivalent  $\leq 40$  mg/d. Pain medications were discontinued during washout (1-7 d) to induce pain-flare (average 24-hour pain intensity score  $\geq 5$ ; 0=no pain; 10=worst pain). Dose was titrated with ALO-01, 20 mg to 80 mg BID, to effective tolerated dose (average pain score  $\leq 4$  with minimum 2-point decrease from baseline). Patients were randomized to ALO-01 at final titrated dose or tapered to placebo BID for the 12-week maintenance-phase. Patients recorded daily pain scores in electronic diaries. There were 344 patients (62.9%) who completed titration-phase and were randomized.

**Results:** Responder rate, defined as  $\geq 30\%$  improvement from titration baseline for in-clinic average pain, was 58.0% at conclusion of titration period. Among those continuing into maintenance-phase, responder rate (titration baseline to week 12) was greater for ALO-01 (72.5%) vs. those tapered to placebo (57.8%;  $p=0.005$ ). Most common adverse events were constipation and nausea during titration, and diarrhea and nausea during maintenance-phase (both ALO-01 and placebo).

**Conclusions:** Results indicate that treatment with ALO-01 resulted in a significantly greater responder rate than with placebo, based on BPI average pain scores, among patients with chronic, moderate-to-severe pain due to osteoarthritis.

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**Disclosure:** This study was supported by Alharma Pharmaceuticals, LLC.

## Pediatric Pain Management

**76. Title:** Effects of children's gender, race, and attractiveness on nurses' pain management decisions

**Presenter:** Ruth Griffin, DNSc, RN

**Biography:** A psychiatric nurse with 30 years of clinical and research management experience, Dr. Griffin conducted this psychosocial pain research as part of her doctoral dissertation at Columbia University.

**Co-presenters:** Denise F. Polit, PhD, President of Humanalysis, Inc. in Saratoga Springs, New York, and Adjunct Professor at the Griffith University School of Nursing in Queensland, Australia; Mary W. Byrne, RN, PhD, MPH, FAAN, Professor at the Columbia University School of Nursing

**Abstract:**

**Objective:** To examine whether nurse perceptions of pain and pain management decisions were affected by stereotypes of school-aged children with varying gender, race, and attractiveness.

**Methods:** 700 randomly-selected RNs were sent study packets with three vignettes, and pain assessment and treatment questions. 334 nurses responded. The vignettes varied on one independent variable (gender, race, level of attractiveness) at a time, while the child's pain and other characteristics remained constant, creating an experimental design. Pain management decisions were assessed by the total amount of analgesic the nurses administered, timing of the analgesic, the number of nonpharmacological procedures recommended, and whether the nurses would involve the family and/or contact the physician.

**Results:** Using nursing characteristics that correlated significantly with pain management-dependent variables as covariates, the analyses of covariance showed no differences between boys and girls, African American and Caucasian children, or attractive and plain children, with regard to nurses' decision on mean dose of analgesic and nonpharmacological interventions. Pain perception was perceived as slightly higher for the less attractive child (VAS 95.5 vs. 93.4  $p=.03$ ), but did not influence pain management decisions. Nurse practitioners and non-nurse practitioners rated children's pain similarly, but nurse practitioners dispensed significantly higher doses of medication ( $t$  2.20,  $p=.02$ ). Nurses with a personal pain history gave more pain medication than nurses without this history ( $t$  1.98,  $p=.04$ ). Nurses' race ( $t$  2.41,  $p=.02$ ) and current working status ( $t$  1.96,  $p=.05$ ) influenced significant differences in the number of nonpharmacological methods. Some nonpharmacological interventions varied by child's gender and race. Nurses used

television, video, or electronic games much more frequently with boys than girls. In contrast, nurses encouraged girls to read to themselves for comfort more frequently than boys (13.5% vs. 6.7%,  $p=.04$ ), and they rocked and swaddled the girls more than the boys.

**Conclusions:** Most importantly, children were treated effectively for their pain, and stereotyping does not seem to be a major concern in nurses' treatment of pain in school-aged children. However, stereotyping was more likely to occur in nurses that were not nurse practitioners; therefore, it would be beneficial to address stereotyping with nurses in early stages of their education, and in the registered nurse scope of practice.

**77. Title:** Multidisciplinary pain centres for children: A study across Canada

**Presenter:** Mélanie Racine

**Biography:** Ms. Racine is a Ph.D. candidate in clinical psychology at the University du Québec à Montréal. Her research interests are in assessment and management of chronic pain.

**Abstract:**

**Objective:** To examine the services currently offered by multidisciplinary pain treatment facilities (MPTFs) dedicated for pediatric chronic pain management across Canada.

**Methods:** A MPTF was defined as a clinic that advertised specialized multidisciplinary services for the diagnosis and management of chronic pain and had a minimum of three different health care disciplines (including at least one medical specialty) available and integrated within the facility. The search method included approaching all hospital and rehabilitation centre administrators in Canada. Designated investigators were responsible for confirming and supplementing MPTFs from the preliminary list in their respective provinces. Administrative leads at each eligible MPTF were asked to complete a detailed questionnaire on their infrastructure, clinical, research, teaching and administrative activities. Only MPTFs dedicated to pediatric populations were included.

**Results:** Only 5 centres surveyed had dedicated pediatric MPTFs, all located in major cities in five different provinces. While the median wait time was 4 weeks, it could be as long as 9 months in one MPTF. Headache and neuropathic pain were the most commonly-treated pain syndromes. All MPTFs included physicians, nurses, and psychologists, and used a rehabilitation model that incorporated a wide variety of pharmacological, psychological, and physical therapies. All centres provided training for medical and other healthcare professionals, and 3 of the 5 centres conducted research. Government funding was the major source of funding for patient services and overhead costs.

**Conclusions:** There are very few pediatric MPTFs in Canada. These facilities exist in five of ten provinces, each within large urban centres. Limited accessibility leads to variable and pro-longed wait times for pediatric patients suffering from chronic pain.

**78. Title:** Impact of pediatric venous access pain: Nurse perceptions

**Presenter:** Jeanne J. Venella, RN, MS, CEN

**Biography:** With more than 25 years of experience in pediatric emergency nursing services, Ms. Venella is respected within the Emergency Nurses Association and has lectured nationally and locally on numerous topics in emergency nursing. She is also a consultant with Blue Jay Consulting, LLC.

**Co-presenters:** Rhonda Morgan, MSN, CEN, CNRN, CCNS, Vice President of Patient Care Services at Holston Valley Medical Center, TN; AnnMarie Papa, MSN, RN, CEN, CNA, BC, Director of Emergency Services at Doylestown Hospital, PA; Terri Voepel-Lewis, MSN, RN, Clinical Nurse Specialist in the Department of Anesthesiology, Pediatrics Section, at the C.S. Mott Children's Hospital, MI; Anne Marie Frey, RN, BSN, CRNI, Pediatric Infusion Therapy Consultant at Pediatric Nurse Consultants, Inc., Clinical Nurse Level IV in Vascular Access Service: I.V. Team at the Children's Hospital of Philadelphia; William T. Zempsky, MD, Associate Director, Pain Relief Program, Connecticut Children's Medical Center; Carole Siegel, PhD, Director of Statistics and Services and Research Division at the Nathan S. Kline Institute for Psychiatric Research, Research Professor in the Department of Psychiatry at New York University; Eugene Laska, PhD, Director of the World Health Organization Collaborating Center for Research and Training in Mental Health Program Management and the Statistical Sciences Laboratory of the Statistic and Services Research Division at the Nathan S. Kline Institute for Psychiatric Research, Research Professor at New York University

**Abstract:**

**Background:** Pediatric inpatients rate IV line placement as one of the leading causes of procedure-related pain in the hospital. An understanding of how nurses are impacted by poorly managed peripheral venous access pain is not well described.

**Objective:** To determine nurse perspectives on the management of pediatric peripheral venous access pain, and its impact on the hospital experience for patients, families, and nurses.

**Methods:** A survey was e-mailed to members of the Emergency Nurses Association, the Infusion Nurses Society, and the Society of Pediatric Nurses asking them to rate the importance of peripheral venous access pain management; characterize the effect of a needlestick procedure on patient and nurse satisfaction; and evaluate available pharmacologic and nonpharmacologic interventions.

**Results:** A total of 2187 nurses completed the survey. Respondents indicated that improved peripheral venous access pain management is associated with improved nurse job performance (91%), nurse job satisfaction (81%), and the hospital experience for children and families (97%). Almost all nurses agreed that inserting an IV into a fearful, anxious child can be challenging and that children undergoing a peripheral venous access procedure require restraints 74% of the time. Pharmacologic interventions are reportedly used only 29% of the time, but nurses estimated 72% of patients experience distress and anxiety when a topical local anesthetic is not utilized. Primary reasons for not using a topical local anesthetic (in rank order) included slow onset, vasoconstriction, no physician authorization, and treatment delays.

# POSTER ABSTRACTS

**Conclusions:** Survey results suggest that nurses perceive improved peripheral venous access pain management in children positively impacts the hospital experience for nurses, patients, and families. Current treatment options are not routinely used. Development of topical local anesthetics that are fast-acting, improved access to available options, and staff education might improve the use of pharmacologic agents in this setting, thus enhancing the perceived hospital experience for nurses, patients, and families.

**Disclosure:** This survey was supported by Anesiva, Inc.

## Psychology of Pain

**79. Title:** Psychopathology in adults with childhood chronic abdominal pain

**Presenter:** Joy E. Beck, PhD

**Biography:** Dr. Beck is a clinical psychologist at Vanderbilt Children's Hospital. Her research and clinical interests focus on applying a developmental psychopathology perspective to chronic pain and functional somatic symptoms.

**Co-presenters:** Kirsten Haman, PhD, Research Assistant Professor in Adult Outpatient Psychiatry at Vanderbilt University Medical Center; Judy Garber, PhD, Professor in the Department of Psychology and Human Development at Peabody College of Vanderbilt University; Lynn S. Walker, PhD, Director of the Division of Adolescent Medicine and Behavioral Science in the Department of Pediatrics at Vanderbilt University School of Medicine

**Abstract:**

**Background:** Children with chronic abdominal pain (CAP) may experience elevated levels of anxiety, depression, and other symptoms of internalizing disorders. However, little data exist as to whether these disorders remit, persist, or even develop further over time.

**Objective:** As part of an ongoing longitudinal study, the current study examines rates of psychiatric disorders in adults who had been diagnosed with CAP during childhood and in healthy controls.

**Methods:** 32 young adults were interviewed, using a structured diagnostic interview, the Anxiety Disorders Interview Schedule for DSM-IV (ADIS). Interviewers were blind to whether the participants had a history of CAP as children (n=21) or had been healthy control subjects (n=11).

**Results:** Adults with a history of CAP were more likely to have met criteria for a psychiatric diagnosis during their lifetime than healthy controls (71.5% vs. 45.5%). A wide range of psychopathology was noted in both groups. In the CAP sample, 47.6% of had a lifetime diagnosis of mood disorder, 47.6% had a lifetime diagnosis of anxiety disorder, and 28.5% had a lifetime diagnosis of substance use disorder. In contrast, 45.5% of the control group had a lifetime diagnosis of mood disorder, 18% had a lifetime diagnosis of anxiety disorder, and 18% had a lifetime diagnosis of substance use disorder. A higher rate of anxiety disorders was reported by the former CAP patients.

**Conclusions:** The experience of CAP in childhood may predispose individuals to experience anxiety even after CAP improves or remits. However, it should be noted that initial levels of psychopathology in

childhood were unknown and may have preceded childhood CAP. Future research should focus on identifying risk factors that predispose CAP patients to mental health disorders and evaluating the impact of mental health treatment on the course of chronic pain.

**80. Title:** Is there a synergy of pain and PTSD on quality of life?

**Presenter:** Joshua D. Clapp

**Biography:** Mr. Clapp is a doctoral student in clinical psychology at SUNY Buffalo. His research interests include physiological factors related to Posttraumatic Stress Disorder with an emphasis on posttrauma emotional deficits.

**Co-presenters:** J. Gayle Beck, PhD, Department of Psychology at the University of Memphis; Sarah A. Palyo, MA, clinical psychology doctoral student on pre-doctoral internship at the VA Palo Alto Health Care System; DeMond M. Grant, Department of Psychiatry at the University of Illinois, Chicago

**Abstract:**

**Background:** Although models have been proposed to explain common factors that maintain comorbid pain and PTSD, the exact nature of the relationship between these two conditions and their impact on quality of life (QOL) is unknown.

**Objective:** The aim of the present investigation was to examine the unique and interactive effects of PTSD and pain on role functioning and life satisfaction—two important domains of QOL.

**Methods:** The study utilized a help-seeking sample of motor vehicle accident (MVA) survivors whose accidents resulted in symptoms of comorbid PTSD and pain (n=192). Hierarchical regression models were used to examine the relationship between four PTSD symptom clusters, pain, and the interaction of each cluster and pain on role functioning and life satisfaction separately.

**Results:** Results of these analyses revealed a significant interaction of pain and emotional numbing on role functioning ( $\beta = 0.19, p=.02$ ), suggesting a multiplicative effect on this domain of QOL.

Decomposition of this interaction revealed a negative association between numbing and functioning at low levels of pain ( $\beta = -0.57, p<.001$ ) but no relationship at higher levels ( $\beta = -0.18, p=.11$ ). A marginal interaction of pain and hyperarousal also was noted for life satisfaction ( $\beta = -0.21, p=.06$ ). Decomposition of the interaction effect revealed a marginal association between hyperarousal and decreased satisfaction only at high levels of pain ( $\beta = -0.26, p=.06$ ). A main effect of emotional numbing on decreased life satisfaction also was observed in this model ( $\beta = -0.54, p<.001$ ), suggesting a unique influence of numbing.

**Conclusions:** Consistent with conceptualizations proposing a dynamic relationship between pain and PTSD, the results of the current study suggest that the synergistic relationship of these factors varies across domains of QOL. These data indicate that interventions targeting *both* physical pain and psychological trauma—particularly symptoms of emotional numbing—may be central to improving QOL in patients with comorbid pain and PTSD.