96 A Multicenter, Open-Label Trial to Assess the Safety and Tolerability of a Single Intravenous Loading Dose of Lacosamide Followed by Oral Maintenance as Adjunctive Therapy In Patients With Partial-Onset Seizures

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Study Objectives: An IV loading dose of lacosamide is desirable when rapid titration is necessary, but current dosing instructions recommend a starting dose of 50 mg twice a day followed by weekly upward titration to the therapeutic target dose. This trial examined the safety and tolerability of a 15-minute intravenous (IV) lacosamide loading dose, followed by oral maintenance treatment at common target doses, in patients with partial-onset seizures (POS).

Methods: Patients were 16-60 years old with POS who were taking 1-2 AEDs but had not previously taken lacosamide. Consecutive 25-subject cohorts were given three progressively increasing doses of lacosamide (200 mg, 300 mg, and 400 mg) administered IV over 15 minutes. Patients received the loading dose followed 12 hours later by the equivalent daily dose that was administered orally twice daily for 6.5 days. Safety and tolerability were assessed after each cohort before enrollment into the next highest dose cohort. A fourth cohort of 25 subjects repeated the 300 mg dose to provide safety data on 50 subjects at the highest well-tolerated dose at this infusion duration. Safety evaluations included adverse events, 12-lead ECGs, vital signs and laboratory parameters. Lacosamide and AED plasma concentrations were measured. Data were analyzed on an intent-to-treat basis. Adverse events were also summarized on an as-treated basis.

Results: Two subjects in the repeat 300 mg cohort received 400 mg infusions; therefore, 25 subjects received lacosamide 200 mg, 48 received lacosamide 300 mg, and 27 received lacosamide 400 mg. Within the first 4 hours after the start of infusion, neurological adverse events were most common. These adverse events tended to be dose dependent, including dizziness (4%, 17%, and 44% in the 200 mg, combined 300 mg, and 400 mg groups, respectively), somnolence (0%, 17%, 26%), nausea (0%, 4%, 19%), and diplopia (4%, 0%, 11%). Seven patients withdrew from the trial, all due to adverse events; 3 (6%) from the 300 mg cohorts, and 4 (16%) from the 400 mg cohort. Four patients withdrew due to at least one AE that started within 4 hours of the IV infusion and 3 withdrew due to AE after oral dosing started.

Conclusion: IV loading doses of 200 mg and 300 mg lacosamide administered over 15 minutes were best tolerated. The 400 mg loading dose was less well tolerated due to a higher frequency of adverse events.

97 Utility of Wet Prep In Predicting Cervical Infections In Women

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Study Objective: Patients presenting with gynecological complaints is common in the emergency department. However, diagnosing Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (NG) cervical infections can be difficult in the emergency department without real time testing and history and physical is known to be notoriously unreliable. We evaluated the utility of the wet prep (present of either white cells or Trichomonas vaginalis (TV)) in diagnosing CT and/or NG.

Methods: A retrospective chart review was performed at a single academic hospital. Patients between the age of 18 to 55 were included who had a chief complaint that would require a pelvic examination and had concurrent testing for gonorrhea and chlamydia via polymerase chain reaction technology (DNA probe). Wet prep mounts were analyzed by a trained technician in the lab and reported as white cells present (none, few, moderate, or many) and the presence of TV. 6 months of data were analyzed from December 2007 to May 2008. Chi-square analysis was used to compare presence of white cells and TV in predicting CT and/or GC.

Results: 1043 encounters were reviewed. A total of 158/1043 (15.1%) patient encounters were positive for CT and/or NG (CT: 98/158, 62%; GC: 35/158, 22%; CT+GC: 25, 16%). 1033 wet prep results were available for analysis. 117/1033 (11.3%) were positive for TV. For those positive with TV, 21/117 (18%) were positive for CT and/or GC. For those who did not have TV, 136/916 (14.8%) were positive for CT and/or GC (Chi-square = 0.55, p = 0.49). 257/1033 (24.9%) had moderate/many white cells present on the wet prep mount. For those with "moderate/many" white cells present on wet prep, 53/257 (20.6%) were positive for CT and/or GC. For those with "few/none" white cells present on wet prep, 104/776 (13.4%) were positive for CT and/or GC (Chi-square = 7.26, p = 0.007; OR = 1.68 [95% CI 1.16-2.42]).

Conclusion: Patients who present with a gynecological complaint that are eventually diagnosed with CT and/or GC, TV is an unreliable marker for diagnosis. However, having moderate to many white cells present on wet prep may slightly increase the probability of CT and/or GC. Adjunct testing using wet prep is not reliable in helping make a diagnosis of CT and/or GC in the emergency department.

EMF-1 Combination Therapy for Ischemic Brain Injury After Cardiac Arrest

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This project focuses on evaluating combination therapy for global brain ischemia after resuscitation from cardiac arrest. The complexity of brain ischemia indicates that combination therapy will be required to intervene in the cascade of multiple, independently-lethal processes that ultimately result in neuronal death. We hypothesize that combination therapy utilizing hypothermia and ZGF-1, multiply-targeted to excitotoxicity, oxidative stress, and apoptosis, will improve neuronal survival and neurobehavioral outcome after transient global brain ischemia, to a degree greater than either treatment alone.

Our specific aims, therefore, are focused not on the elucidation of mechanisms of neuronal death, but on evaluating the neuroprotective effect of combined IGF-1 and hypothermia following transient global brain ischemia. It is therefore critical to emphasize that, while this approach is based on many hard-won mechanistic insights into brain ischemia--including discoveries made by this group--this is not a mechanistic research project, but a preclinical, translational investigation. No mechanistic aims are proposed. Rats will be subjected to 8 minutes of transient global brain ischemia followed by administration of IGF-1 and hypothermia during reperfusion. Following the criteria recommended by the Stroke Therapy Academic Industry Roundtable (STAIR) consensus panel, we will generate dose-response curves of tissue-level effects at 6 hours of reperfusion, measuring biochemical pathways targeted by IGF-1 and hypothermia. Tissue-level assessment will determine whether neurons are being saved. Finally, we will determine whether combination therapy results in improvements in neurological function.

This structured approach, using simultaneous measurement of biochemical, structural and functional outcomes, offers the best opportunity to develop effective clinical interventions. Combination therapy has been identified as a critical need by the National Institute of Neurological Disease and Stroke. The results of this study, if positive, will be incorporated as preliminary data in a proposal for Federal funding with the ultimate goal of clinical studies for combination therapy.

EMF-2 Prediction of Moderate/Severe Post-Thrombophlebitic Syndrome After Acute Deep Venous Thrombosis of the Leg

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Significance: Deep venous thrombosis (DVT) is a common disorder with an estimated lifetime incidence of 2% to 5%. The majority of published research on DVT has focused on prevention of short-term complications of this disease including pulmonary embolus and recurrent thromboembolism which can life-threatening. Conversely, relatively few studies have measured the long-term complications of DVT including post-thrombophlebitic syndrome (PTS). Not only does this complication impair lifestyle, independence, and perception of wellness, but it also incurs a large cost in terms of health care dollars and lost work productivity. The ED represents an efficient and appropriate platform to implement preventive measures for severe complications from DVT. However, the first step toward devising and implementing strategies to help decrease the morbidity of PTS, its incidence must be defined, and no prior study has done so in an ED outpatient population The hypothesis of this project is that: 1. Emergency department patients diagnosed with a first-time deep venous thrombosis (DVT) of the lower extremity have a >5% probability of developing disabling thrombophlebitis. 2. The blood concentration of circulating.products of c~llagenolyks will predict severity of thrombophlebitis in patients with acute DVT. Specific Aims: 1. This project will develop a system to identify ED and other outpatients with recently diagnosed DVT in a setting to allow longitudinal follow-up. 2. Using banked blood samples, provided by the project mentor from separate projects, establish preliminary data to assess the prognostic significance of a peptide fragment produced by the action of inducible matrix metalloproteinases (MMP) on type I and III collagen. Methods: This methodology