

[2003 Fall A7] A phase II, multi-center, randomized, double-blind, placebo-controlled, crossover study of CJC-1008, A long-acting, parenteral, opioid analgesic, in the treatment of postherpetic neuralgia

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Introduction: Conjuchem Inc. has developed a technology that enables the covalent bonding (conjugation) of a therapeutic drug to an endogenous target protein and at the same time retaining a highly concentrated, targeted therapeutic activity. Conjuchem has applied the technology platform to the selective opioid receptor peptide Dynorphin A to create a new chemical entity, CJC-1008. It is hypothesized that CJC-1008 will provide pain relief with an improved safety profile and extended duration of action as compared to conventional opioids. The primary objective of this study was to evaluate the preliminary efficacy of a single dose of CJC-1008 as compared with placebo by measuring change in overall pain intensity over time (up to 28 days) in patients with post herpetic neuralgia.

Methods: This was a Phase II, randomized, double-blind, placebo-controlled, crossover study comparing the efficacy of a single IV dose of CJC-1008 at 3mg/kg to placebo in patients with PHN. After meeting all eligibility criteria at screening (visit 1), patients who were taking opiate analgesics entered a 2-7 day opiate washout period. Following the washout period, patients with a minimum pain intensity score of 45 mm for overall pain intensity were assigned 1:1 to receive active study medication or placebo. After dosing, the following took place every 15 minutes for the first hour, then at 2, 3, 4, 6, and 8 hours postdose, then during return visits to the study site after 2, 7, and 28 days (as necessary), precrossover and exit visits: 1) Overall pain intensity (100 mm VAS); 2) Pain intensity (100 mm VAS) for each individual PHN type; 3) Categorical overall pain intensity (6-point Likert); 4) Categorical pain relief (6-point Likert); 5) Adverse events. At 28 days after dosing, or as soon as 2 days, at such time as PHN pain intensity returned to baseline (i.e. VAS >45 mm) and/or at patients first request for rescue analgesia other than acetaminophen, patients were to crossover to the alternate treatment and be followed on the same schedule.

Results: A total of 32 patients entered the study and were randomized to treatment from the 4 study centers (Wallace-12, Moulin-8, Clark-7, Wasserman-5). Thirty patients received study treatment and 26 patients completed the study. A total of 29 of the 30 patients (96%) experienced at least 1 treatment-emergent adverse event (AE) during active drug treatment while 14 of 27 patients (52%) reported such AEs during placebo treatment. Of the AEs occurring within the first 8 hours of dosing, 97% were reported during treatment with active drug and 3% were reported during treatment with placebo. The majority of these AEs were mild in intensity.

Discussion: This study provides evidence of a greater analgesic effect of CJC-1008 compared to placebo in patients with PHN. However, the effect only lasted through 8 hours post dose and diminished by 24 hours. This study provides evidence of a peripheral action of dynorphin since CJC-1008 does not cross the blood-brain barrier. The drug commonly caused local infusion reactions that were generally mild and transient.