A Phase III Randomized, Placebo-Controlled, Double Blind Study of Intravenous Calcium/Magnesium to Prevent Oxaliplatin-Induced Sensory Neurotoxicity

Purpose of Study:
1. To determine whether CaMg infusions can prevent or ameliorate chronic, cumulative neurotoxicity associated with oxaliplatin.
2. To determine whether CaMg infusions can increase the cumulative oxaliplatin doses that can be delivered without chronic neurotoxicity.
3. To determine whether CaMg infusions can ameliorate the acute neuropathy associated with oxaliplatin.
4. To determine whether CaMg infusions cause any adverse events.
5. To investigate whether CaMg infusions influence quality of life, fatigue, and activities of daily living (ADLs).
6. To determine if polymorphisms in the GSTP1 gene predict for early onset of oxaliplatin-induced neurotoxicity

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Study Status/Accrual: This study was opened on 01/13/2006 and was closed on 06/19/2007 with a final accrual of 104 patients. The final complete Status Report was produced Spring, 2008.


Abstract: Purpose: Cumulative sensory neurotoxicity (sNT) is the dose-limiting toxicity of oxaliplatin, which commonly leads to early discontinuation of oxaliplatin-based therapy in the palliative and adjuvant settings. In a nonrandomized, retrospective study, intravenous (IV) calcium/magnesium (Ca/Mg) was associated with reduced oxaliplatin-induced sNT. Methods: Patients with colon cancer undergoing adjuvant therapy with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX) were randomly assigned to Ca/Mg (1g calcium gluconate plus 1g magnesium sulfate pre- and post-oxaliplatin) or placebo, in a double-blinded manner. The primary end point was the percentage of patients with grade 2 or greater sNT at any time during or after oxaliplatin-based therapy by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE; version 3) criteria. An oxaliplatin-specific sNT scale and patient questionnaires were also used to assess sNT. After 104 of 300 planned patients were enrolled, the study was closed. This was due to preliminary reports from another trial that suggested that Ca/Mg decreased
treatment efficacy; these data were subsequently found to be incorrect. **Results:**
Overall, 102 patients were available for analysis. Ca/Mg decreased the incidence of chronic, cumulative, grade 2 or greater sNT, as measured by NCI CTCAE (P = .038) and also by the oxaliplatin-specific sNT scale (P = .018). In addition, acute muscle spasms associated with oxaliplatin were significantly reduced (P = .01) No effect on acute, cold-induced sNT was found. No substantial differences in adverse effects were noted between Ca/Mg and placebo. **Conclusion:** Despite early termination and decreased statistical power, this study supports IV Ca/Mg as an effective neuroprotectant against oxaliplatin-induced cumulative sNT in adjuvant colon cancer.