NCCTG-N08CB

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

ClinicalTrial.gov Identifier: NCT01099449

Study Background

Trial Description

RATIONALE: Chemoprotective drugs, such as calcium gluconate and magnesium sulfate, may prevent neurotoxicity caused by oxaliplatin. It is not yet known which administration schedule of calcium gluconate and magnesium sulfate is more effective in preventing neurotoxicity.

PURPOSE: This randomized phase III trial is studying different administration schedules of calcium gluconate and magnesium sulfate and comparing how well they work in neurotoxicity in patients with colon cancer or rectal cancer receiving oxaliplatin-based combination chemotherapy.

Arms:

Arm I: (Experimental): Patients receive calcium gluconate and magnesium sulfate IV over 30 minutes immediately before and after oxaliplatin administration (part of FOLFOX chemotherapy comprising leucovorin calcium, fluorouracil, and oxaliplatin).

Arm II: (Placebo Comparator): Patients receive placebo IV over 30 minutes immediately before and after oxaliplatin administration (part of FOLFOX chemotherapy).

Arm III: (Experimental): Patients receive calcium gluconate and magnesium sulfate IV over 30 minutes immediately before and placebo IV over 30 minutes immediately after oxaliplatin administration (part of FOLFOX chemotherapy).

Objectives:

- OBJECTIVES:
- Primary
  - To determine whether 2 schedules of calcium gluconate and magnesium sulfate infusions (given before and after chemotherapy or just before chemotherapy) can prevent or ameliorate chronic, cumulative oxaliplatin-induced sensory

neurotoxicity in patients with colon or rectal cancer receiving adjuvant FOLFOX chemotherapy comprising leucovorin calcium, fluorouracil, and oxaliplatin.

- Secondary
  - To determine whether these 2 infusion schedules can increase the cumulative oxaliplatin doses that can be delivered without dose-limiting chronic neurotoxicity.
  - To determine whether these 2 infusion schedules can ameliorate acute neuropathy associated with oxaliplatin.
  - To determine whether these 2 infusion schedules cause adverse events.
  - To investigate whether these 2 infusions schedules influence patient quality of life.
  - To describe baseline and post-treatment neurological quantitative sensory testing abnormalities in the study participants.
- Tertiary
  - To explore if polymorphisms in the GSTP1, GSTM1, ERCC2, and XRCC1 genes are associated with early onset of oxaliplatin-induced neurotoxicity.
- OUTLINE: This is a multicenter study. Patients are stratified according to age (< 65 years vs ≥ 65 years), gender, regimen (FOLFOX4 vs modified FOLFOX6 vs other), and stage of disease (II vs III vs IV). Patients are randomized to 1 of 3 treatment arms.
  - Arm I: Patients receive calcium gluconate IV and magnesium sulfate IV over 30 minutes immediately before and after oxaliplatin administration (part of FOLFOX chemotherapy comprising leucovorin calcium, fluorouracil, and oxaliplatin).
  - Arm II: Patients receive placebo IV over 30 minutes immediately before and after oxaliplatin administration (part of FOLFOX chemotherapy).
  - Arm III: Patients receive calcium gluconate and magnesium sulfate IV over 30 minutes immediately before and placebo IV over 30 minutes immediately after oxaliplatin administration (part of FOLFOX chemotherapy).
- In all arms, courses repeat every 14 days for 6 months in the absence of disease progression or unacceptable toxicity.
- Blood samples are collected before the second course of treatment for translational research.
- Patients complete questionnaires on side effects, quality of life, and chemotherapy-induced peripheral neuropathy periodically.
- After completion of study treatment, patients are followed up at 3, 6, 12, and 18 months.

Study Milestones:

Start date: June 2010

Primary Completion Date: March 2013

Publication Information:

Analysis Type: Primary

PubMed ID: 24297951

Citation: J Clin Oncol. 2014 Apr 1;32(10):997-1005. doi: 10.1200/JCO.2013.52.0536. Epub 2013 Dec 2.

Associated Datasets: Associated Datasets: NCT01099449-D1-Dataset.csv (table1), NCT01099449-D2-Dataset.csv (figure1), NCT01099449-D3-Dataset.csv (figure2), NCT01099449-D4-Dataset.csv (figure3), NCT01099449-D5-Dataset.csv (gr2neurotox_fig45), NCT01099449-D6-Dataset.csv (figure6), NCT01099449-D7-Dataset.csv (table2)

Dataset Information:

Dataset Name: NCT01099449-D2-Dataset.csv (figure1)

Description: Dataset NCT01099449-D2-Dataset.csv (figure1) is one of 7 datasets associated with PubMed ID 24297951. This dataset contains the information in figure 1: CONSORT diagram.

Data can be used to approximate published study findings, but exact reproduction of previous manuscripts may not be possible in some cases (e.g., when data must be modified for de-identification purposes or have undergone further data cleaning).

NCT01099449-D2-Dataset.csv (figure1) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
No Baseline Sensory Score	nobsl	Patient has baseline sensory score, Patient does not have baseline sensory score	
Only 1 cycle of sensory data	only1	Patient has more than one cycle of sensory AUC, Patient only has one cycle of sensory AUC data	
Patient ID	patref		
Arm	arm	CA/MG Before and After Chemo, CA/MG Before and Placebo After, Placebo	
Excluded patients (withdraws and Ineligible)	excluded	Missing=Not Excluded, Withdrew, Ineligible	