



# Duke Clinical Research Institute

## DUKE UNIVERSITY MEDICAL CENTER

### SAFETY SURVEILLANCE

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Date: 21Sep2006

To all investigators in TACT:

RE: SAE Report # 10007, Serious Adverse Event: NEPHROLITHIASIS

Dear Doctor,

In accordance with the Good Clinical Practice and specific national regulatory requirements, we wish to inform you of an unexpected, serious adverse event which occurred in TACT, "A multi-site, randomized, double-blind, placebo-controlled trial investigating the efficacy and safety of EDTA (ethylene diamine tetra-acetic acid) chelation therapy in individuals suffering from Coronary Artery Disease (CAD)".

The current case concerns a patient in the above trial who experienced NEPHROLITHIASIS. This 51 year old female with a history of angina pectoris, hypertension, hypercholesterolemia, cigarette smoking, coronary artery bypass graft surgery, revascularization of the lower extremities, and revascularization of the carotid arteries, was randomized to EDTA chelation or placebo on 21Jun2005. The patient had received a total of 31 intravenous infusions of chelation solution or placebo to date. The patient received infusions from 01Jul2005 through 13Jul2006. The patient had reached the maintenance infusion phase of study dosing. The last dose of study drug was infusion 31, administered on 13Jul2006 from 10:30 hours to 13:45 hours.

The serious adverse event of kidney stone occurred on 07Sep2006. The patient experienced abdominal pain, vomiting, and nausea and was seen in the emergency room. The patient was diagnosed with a kidney stone and was admitted to the hospital. The investigator assessed that a causal relationship between the study medication and the adverse event was possible. The patient developed a left ureteral calculus while enrolled in the study which involves regular infusions of chelation agents and the intake of vitamins. The investigator assessed it is possible that one or more of these agents could promote kidney stone formation. My review of the Investigational Drug Brochure as well as the available literature suggests that EDTA therapy may play a role in the lysis of preexisting stones by the dissolution of the calcium matrix. While conceivably the 24 hour urine calcium excretion may rise following the administration of EDTA, the literature does not support that in the presence of EDTA portends an increased risk of precipitation. It is, however, possible that the use of high dose vitamin C may contribute to the risk of nephrolithiasis. I do not believe that it is likely that the EDTA contributed to the risk of nephrolithiasis but do believe that high dose vitamin C may contribute.

We are distributing an investigator alert, since NEPHROLITHIASIS is not specifically mentioned in the TACT Investigator's Brochure. We will keep you informed if further relevant information becomes available on this type of adverse event. Please submit a copy of this letter to your IRB for review. Please file a copy of this letter, along with any response, in your regulatory binder. If your IRB requests that the informed consent be changed, please do so and submit a copy of the new consent to your site manager or monitor for approval before implementing.

If you have any questions or further concerns regarding this SAE, please contact me at (919) 668-8008 (phone), [szcze001@mc.duke.edu](mailto:szcze001@mc.duke.edu) (e-mail), or (919) 668-7128 (fax).

Yours sincerely,

A handwritten signature in cursive script, appearing to read 'L. Szczech'.

Lynda Szczech, MD,  
DCRI Medical Monitor