



# Duke Clinical Research Institute

## DUKE UNIVERSITY MEDICAL CENTER

### SAFETY SURVEILLANCE

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Date: 22 November 2006

To all investigators in TACT:

RE: SAE Report # 10008, Serious Adverse Event: MALAISE

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 MALAISE. This 61 year old male with a history of coronary artery disease, angina pectoris, diabetes, hypertension, hypercholesterolemia, cigarette smoking, fractures since age 50 and percutaneous coronary intervention was randomized to EDTA chelation or placebo on 27 March 2006. The serious adverse event of malaise occurred 11 October 2006 at 13:00 hours. The patient was admitted to the hospital approximately 1 1/2 hours after receiving his 24th infusion. According to the site all tests were within normal limits or unchanged from previous assessments. On 15 October 2006, electrocardiogram revealed an abnormal electrocardiogram, normal sinus rhythm, left anterior fascicular block, minimal voltage criteria for left ventricular hypertrophy, non-specific ST and T wave abnormality. When compared with electrocardiogram of 28 July 2006, no significant changes were found. On 15 October 2006, portable chest x-ray revealed the heart size was probably within normal limits with poor inspiration. No infiltrates or effusions were seen. On 16 October 2006, blood cultures were drawn which revealed no growth on 21 October 2006. On 17 October 2006, the patient blood glucose was 215 mg/dL (normal range 70 – 108 mg/dL). On 17 October 2006, the patient underwent a gastric emptying study that showed a normal gastric emptying study, and no gastroparesis was seen. No significant interval change was noted when compared to the prior examination. The patient was discharged on 17 October 2006. On 31 October 2006, the patient underwent adenosine cardiolute stress test. The test impressions were: 1, unremarkable adenosine cardiolute stress test. No ST-T wave changes suggestive of ischemia or significant arrhythmias were noted. 2, no evidence of ischemia was noted on the cardiolute perfusion images. 3, gated spot imaging showed an ejection fraction of 57 percent without any obvious segmental wall motion abnormalities. The patient felt better after not taking the vitamins for 1 week. The patient thinks the symptoms were caused by the vitamins and the infusions and decided to withdraw from TACT. The investigator assessed that a causal relationship between the study medication and the adverse event was possible.

I have reviewed the information available and the assessment of the patient and the investigator. I think that it is appropriate to concur with their statements that this event is related to study participation. Clearly, the event term is not specific with respect to etiology of the event. However, I do not believe that this information is available clinically. This event is therefore reviewed as related and unexpected.

TACT is distributing an investigator alert, since MALAISE 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 the Clinical Coordinating Center at Mt. Sinai for approval before implementing.

If you have any questions or further concerns regarding this SAE, please contact me at (919) 688-8008 (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