# Summary of Proposed TACT2 Ancillary Study

This TACT2 ancillary study aims to investigate the potential links between coronary calcification and the effects of chelation therapy on coronary events.

Background: TACT showed chelation therapy significantly reduced MACE in post-MI patients. Subgroup analyses surprisingly showed that the benefit appeared to be largely if not entirely confined to two subgroups, patients with diabetes, and patients with anterior MI, see below.

Impact of Therapy on 5-Year Kaplan-Meier in *Anterior* MI Patients

HR 0.63 (0.47, 0.86, p=0.003)*
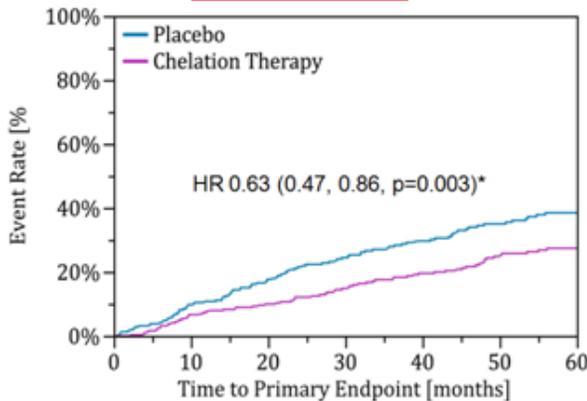
Impact of Therapy on 5-Year Kaplan-Meier in *Non-Anterior* MI Patients
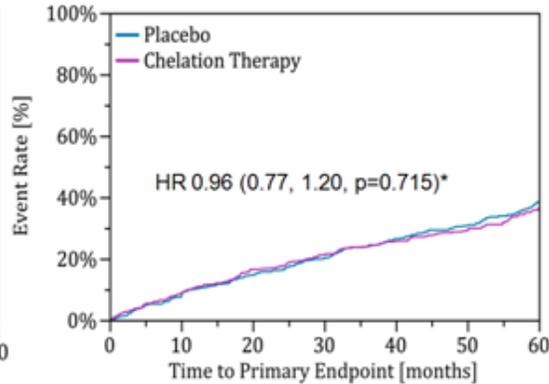
HR 0.96 (0.77, 1.20, p=0.715)*

Kaplan-Meier Estimates of the Primary Composite Endpoint — EDTA Chelation Therapy vs. Placebo — Subset of Patients with Diabetes: Hx, Med Use or Baseline Glucose >=126
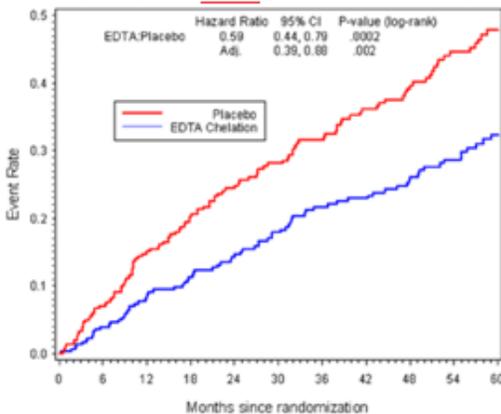
	Hazard Ratio	95% CI	P-value (log-rank)
EDTA:Placebo	0.59	0.44, 0.79	.0002
Adj.	0.39, 0.88		.002

Kaplan-Meier Estimates of the Primary Composite Endpoint — EDTA Chelation Therapy vs. Placebo — Subset of Patients without Diabetes (Hx, Med Use or Baseline Glucose <126)

	Hazard Ratio	95% CI	P-value (log-rank)
EDTA:Placebo	1.02	0.81, 1.28	.8768
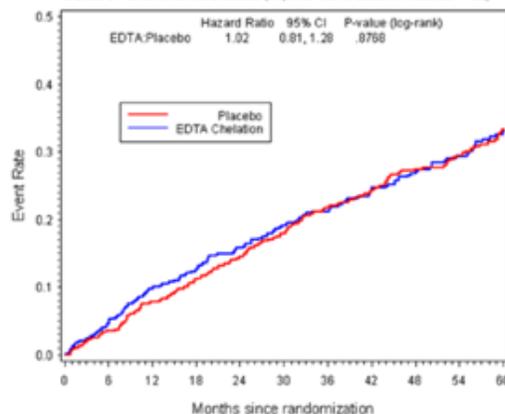
Knowing that coronary calcium score is the most powerful predictor of coronary events, and that 1) patients with LAD disease have a higher coronary calcium score than those without, 2) diabetic patients have a higher coronary calcium score than non-diabetic patients, 3) progression of coronary calcium is a strong predictor of adverse events and that 4) chelation therapy removes calcium from the body, we propose this ancillary study with the following specific aims:

1- Determine if TACT2 patients with higher coronary calcium scores respond more favorably to chelation therapy than those with lower coronary calcium scores.

2- Determine if TACT2 patients with more dense coronary calcification respond more favorably to chelation therapy than others.

3- Determine if chelation therapy reduces the progression of coronary calcification or changes the pattern of coronary calcification, and whether such a change correlates with outcomes.

We propose this ancillary study to be conducted on half of TACT2 patients (600 cases). In our proposal patients will undergo two coronary calcium scans, one at baseline and one at the end of the study around month 12. Large studies such as MESA have shown that progression of coronary calcium score is in average 15% per year. Those who exceed 15% increase in coronary calcium score are at a higher risk of future events. Coronary calcium is noninvasive, does not require injection of any contrast agent, and requires less radiation than mammography. It can be done with multi-slice CT scan available in almost all study centers.

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Relevant references:

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