



## VA COOPERATIVE STUDIES PROGRAM # 424

### Clinical Outcomes Utilizing Revascularization and Aggressive DruG Evaluation

#### Operations Memo No. 27

Date: October 18, 2000  
From: Dr.'s William E. Boden and Robert A. O'Rourke, Co-Chairmen  
Subj: **Inclusion of patients with "classic" or "definite" angina in whom non-invasive testing for myocardial ischemia cannot be readily obtained**  
To: All Study Personnel  
Thru: Trial Leadership

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There are potentially many COURAGE-eligible patients with "classic" or "definite" angina who have angiographically-significant proximal coronary artery disease (CAD), but who have proceeded directly to the cardiac catheterization laboratory without first having had objective evidence of myocardial ischemia documented by an abnormal resting ECG or non-invasive laboratory testing (exercise or pharmacologic). In many instances, the decision to proceed directly to coronary angiography has been dictated by referral practice patterns and the expectation that diagnostic coronary angiography would be obtained expediently to assess the presence or absence of abnormal coronary anatomy.

Presently, the COURAGE Trial inclusion criteria mandate the documentation of myocardial ischemia; COURAGE-eligible patients must have either demonstrable ST-T wave changes in two or more contiguous ECG leads at rest, or have objective evidence of inducible ischemia during exercise or pharmacologic vasodilator stress (exercise-induced ST-segment deviation of at least 0.1 mV; a reversible perfusion defect or wall motion abnormality during stress myocardial perfusion imaging or echocardiography).

In order to broaden patient enrollment and to include appropriate patients with symptomatic CAD who may be suitable candidates for percutaneous coronary intervention (PCI) even in the absence of objective findings of ischemia, we propose to modify the COURAGE Trial inclusion criteria in selected instances whereby patients with subjective symptoms of "classic", or "definite", angina (please refer to Op Memo # 26) may be trial-eligible without objective findings of myocardial ischemia if they meet a more stringent definition of angiographic stenosis in the setting of multivessel CAD.

The following revised definition for trial inclusion will be used for COURAGE-eligible patients who have symptomatic CAD (the principal target population of patients who would be expected to benefit from PCI) but who have no objective evidence of myocardial ischemia.

**All three of the criteria listed below must be met for a patient to be considered COURAGE Trial-eligible:**

- The patient must have symptoms of “classic”, or “definite”, angina, as defined in Op Memo # 26. In brief, patients must display (in the opinion of the investigator or operator) convincing symptomatology of exertional or rest angina that meets the cardinal criteria (character, site & distribution, provocation and duration) described originally by Heberden and Wood, and adopted as the definition of “classic”, or “definite”, angina in the recently-published ACC/AHA Guidelines on both the Management of Chronic Stable Angina and Unstable Angina/Non-ST-Segment Elevation Acute Coronary Syndromes; **and**
- The patient must have a measured 70% or greater angiographic stenosis (caliper-measured or quantitatively-measured) of a proximal epicardial coronary artery that, in the opinion of the operator/investigator, is the culprit vessel responsible for the ischemic syndrome; **and**
- There must be angiographic documentation of significant stenosis (50% or greater) in another coronary artery in addition to the 70% or greater “culprit stenosis”. Thus, the patient must have multivessel (2-3 vessel) CAD.

In summary, the standard COURAGE Trial criteria of defining objective evidence of myocardial ischemia and angiographic CAD (50% or greater in a proximal epicardial coronary artery) remain the principal inclusion criteria for patient recruitment.

For those potentially COURAGE-eligible patients with symptoms of “classic” or “definite” angina who are referred from outlying hospitals or from referring physicians with the stated expectation that they would proceed directly to diagnostic coronary angiography, this change in the trial inclusion criteria should facilitate the enrollment of patients with multivessel CAD who have at least a measured 70% stenosis of a proximal coronary artery.

Please call either of the COURAGE Trial co-chairmen if there is a question.