# The Efficacy of Inacrolide in the Prevention of Acute Stenosis After Angioplasty in Patients with Antichlamydia Antibodies

*Peter Cheung*

### A. Study Purpose and Rationale

In two previous studies, macrolide antibiotics are successful in achieving a fourfold reduction in adverse cardiac events in patients with coronary artery disease. Restenosis after angioplasty occurs in two phases. The acute phase occurs in days and its mechanism appears to involve elastic recoil, intimal flap, mural thrombus, subintimal hemorrhag

ge, and platelet adhesion. The second phase occurs in days to months, peaks at 1-3 months and is coinpleted by 6 months. Mechanism involves neointimal proliferation and vascular remodeling. The two phases may bear similarities and distinctions from the gradual process of atherosclerosis This study will look at whether inacrolide may have similar success in preventing acute stenosis after angioplasty in patients who have antichlamydia antibodies.

### B. Study Design and Statistical Analysis

This is a randomized, double-blind, placebo-controlled study on die effect of inacrolide. Patients who are to undergo cardiac catlicterization either emergently or electively are recruited in die cath lab. Patients are excluded if they are currently taking macrolide, or if macrolide is contraindicatcd (allergy, adverse drug interaction). Once the above criteria is satisfied, they are randomized to receive either iv azithromycin or a placebo.

Patients are screened forinti-chlamydia pneumoniae antibodies. They are subsequently excluded from the study if antibodies are negative, or if antibodies cross-react with antigens from Cblamydia trachomatis or Chlamydia psitticai. During cath, the following characteristics are noted and reported in table I to determine the effectiveness of the randomization process: coronary artery diameter, lesion length, vessel involved (LAD/SVG), pre- and post-procedure degree of stenosis, TIMI, location and complexity of lesions, presence of thrombus, and the use of stent. Patient is also excluded if, upon the completion of cath, it is determined that he should receive CABG.

End points are defined as recurrent chest pain requiring repeat cath, myocardial infarction, emergent CABG, or death. Acute restenosis is studied indirectly by measuring the frequency of end points. Acute restenosis usually are not clinically subtle and require immediate medical attention. To access restenosis angiograpbically would mean subjecting a large number of asymptomatic patients to the risks of repeat angioplasty. The necessity is not warranted. Therefore, only clinical restenosis is assessed. Patients are followed for 3 days after cath. If they are discharged before 3 days, they will follow up within a week for any adverse event that had occurred within 3 days of cath.

A X2 study is performed to evaluate the relative risk of clinical restenosis and 95% confidence interval will be constructed. For patients who undergo a second cardiac cath because of chest pain or myocardial infarction, a subgroup analysis will be performed to evaluate relative risk of angiographic restenosis.

Assuming an event rate of 5%, and risk reduction of 60% with azithromycin, a group of 353 patients are need to provide a statistical power of 80%.

### C. Study Procedures

Participation in the study involves drawing 5cc of blood forantibody study. This blood may be drawn with the other necessary blood test. Participant may also require additional intravenous catheter placement to receive either antibiotic or placebo for 3 days. If a participant is discharged before 3 days, be would be asked to follow-up within I week. A medical history will be taken about any event within the 3 days.

**D. Study Drug**

Azithromycin is an FDA approved antibiotic with a wide range of spectrum against different bacteria. IV azithromycin is also an accepted route of administration. Dosage administered in this study is similar to that used in other clinical setting. Possible adverse side effects include nausea, vomiting, diarrhea, abdominal pain. Very rarely, patient may develop liver and kidney problems. The effect of azithromycin in pregnancy is unknown. It is also unknown whether azithromycin is excreted in breast milk.

**E. Medical Devices**

Not applicable.

**F. Study Questionnaires**

Not applicable.

**G. Study Subjects**

As discussed in section B.

Because subject group should be representative of all patients who are undergoing cath. Patients who are undergoing cath emergently will be included and may be vulnerable. Every attempt would be made to emphasize that refusal to participate will in no way affect the care that the patient will receive.

**H. Recruitment of Subjects**

Patients are recruited in the cath lab while they are awaiting the procedure. At no point will the cath be delayed because of the recruitment process. Patient's primary physician will be identified and will be contacted to determine whether patient is a suitable candidate. Then the patient will be asked by the nurse whether he would be interested in discussing a 3 day antibiotic trial. It will be emphasized that participation is voluntary and doesn't affect his treatment. If the patient agrees, the nature of the study will be explained by the research team.

**I. Confidentiality of Study Data**

Any identifying information will be safeguarded in confidential files within locked cabinets. Each subject would be assigned a study code. Identifying information will be accessed only when additional clinical information is needed.

**J. Potential Conflict of Interest**

Neither the investigator nor the University have any proprietary interest in azithromycin. Nor do they stand to gain financially from the results of this investigation.

**K. Location of the Study**

Study will be conducted entirely within Milstein hospital in the cath lab, CCU, and inpatient ward.

**L. Potential Risks**

Patient may develop an adverse reaction to azithromycin. He may also run a risk of being colonized by resistant bacteria which may render this antibiotic useless for treatment of other conditions. There are also risks of pain, bruising, and a small chance of infection with the placement of additional intravenous catheter.

**M. Potential Benefits**

Ile study is designed to evaluate whether a new treatment modality is available and to help understand the mechanism of disease. Benefits to society may be that the information obtained from this study may evolve into effective treatment. Benefits to individual may be that azithromycin is effective in preventing restenosis, of an artery. However, no benefit is guaranteed.

**N. Alternative Therapies**

Since azithromycin is not used in this study to compare with or substitute for another form of therapy. Patient will receive full and-ischemic therapy as deemed necessary by his cardiologist.

**O. Compensation to Subjects**

There will be no monetary compensation for participating in this study.

**P. Costs to Subjects**

T'here will be no additional costs for participating in this study. Azithromycin will be supplied at no cost. Patient or his insurance company will be required to pay for the routine treatment for his condition.

**Q. Minors as Research Subjects**

Not Applicable.

**R. Radiation or Radioactive Substances**

Not Applicable.