SUPERASPIRINS: NOVEL PRO-DRUGS ARE MORE EFFECTIVE THAN CONVENTIONAL ASPIRIN AND DO NOT CAUSE DIRECT GI TOXICITY

i2 Poster Contributions
Ernest N. Morial Convention Center, Hall F
Monday, April 04, 2011, 3:30 p.m.-4:45 p.m.

Session Title: PCI - Adjunct Pharmacology
Abstract Category: 7. PCI - Adjunct Pharmacology
Session-Poster Board Number: 2513-588

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Background: Although conventional aspirin therapy significantly reduces the incidence of cardiovascular events, myocardial infarction or stroke in patients with previous cardiovascular events, treatment failure is common. Furthermore, the use of conventional aspirin is limited by gastro-intestinal side effects. Novel pro-drug approaches may solve these efficacy/tolerability challenges. We have recently reported synthesis and characterisation of the first true aspirin pro-drugs.

Methods: We evaluated the comparative efficacy of a three novel aspirin pro-drugs versus conventional aspirin at equimolar doses using in-vitro and in-vivo models of platelet aggregation. We examined the comparative topical effects of high doses over three days in rat and rabbit models of GI injury.

Results: Two of the prodrugs were significantly more effective than conventional aspirin in attenuating platelet aggregation in human platelet rich plasma in response to response to adenosine diphosphate, collagen and arachidonic acid. One of these agents was also more effective in inhibiting the activation of human platelets in response to exposure to M59 ovarian cancer cells. In vivo pre-clinical studies show that one of the agents was more effective than aspirin at equimolar doses in the inhibition of TxB2 production. At high doses (30 mg/Kg daily for 3 days) conventional aspirin produced significant ulceration in in-vivo models of gastro-intestinal injury whereas the prodrugs caused no damage at equimolar doses.

Conclusions: The efficacy and safety of conventional aspirin may be improved using two of a family of novel aspirin pro-drugs. This may reduce therapy failure with aspirin and raise the possibility of new applications of this important therapy beyond secondary prevention of cardiovascular disease.