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RISK/BENEFIT ANALYSIS FOR THE USE AND APPROVAL OF THROMBOLYTIC, ANTIARRHYTHMIC, AND HYPOLIPIDEMIC AGENTS

PROCEEDINGS OF THE NINTH ANNUAL SYMPOSIUM ON NEW DRUGS & DEVICES, OCTOBER 27 & 28, 1988

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PREFACE

The Symposium on New Drugs provides a forum for academic investigators, research and development personnel from the pharmaceutical industry and members of the Food and Drug Administration to discuss important clinical research issues. The Ninth Annual Symposium on New Drugs addressed the problem of determining the risk versus benefit for use of three important classes of cardiovascular agents: thrombolytic, antiarrhythmic, and hypolipidemic agents.

The use of thrombolytic agents has become one of the major advances in clinical intensive cardiologic care in the 1980s. While the lysis of clot(s) obstructing a major coronary artery should reverse or prevent the damage of acute myocardial ischemia and infarction, one must carefully consider the potential risks of such agents in regards to their potential benefits. The time when a thrombolytic agent should be administered to maximize benefit as well as how one defines a dose response relationship using intravenous critical care medicines were discussed as important clinical trial issues. The benefit versus risk data on currently available thrombolytic agents was reviewed and the potential roles for adjunctive agents addressed. Overall strategies regarding post-

thrombolytic care and relationships to sudden cardiac death were also detailed. The panel discussion sections provided a comprehensive view of the current thinking of the various participating groups in this Symposium.

Sudden cardiac death remains the number one cause of mortality in western industrialized societies. The potential for antiarrhythmic drug therapy to reverse this epidemic still has not been established; in fact, new antiarrhythmic drugs with better benefit versus risk ratios may be necessary to determine this endpoint. The viewpoints of the Food and Drug Administration as well as clinical academic investigators were reviewed. In addition, the pharmaceutical industry's concern regarding the practicality of developing new antiarrhythmic agents under current guidelines was emphasized.

The potential for preventing or reversing the atherosclerotic process and coronary events by reducing elevated atherogenic lipoproteins has provided an exciting new area for preventive therapy. New recommendations to the medical community regarding criteria for institution of hypolipidemic therapy may substantially influence the nature of clinical trials in this field. Comparative risks versus benefits for

the currently available hypolipidemic agents as well as design issues such as defining endpoints in clinical trials were detailed. Current guidelines to obtain regulatory approval for new lipid lowering agents were also discussed.

We believe the positions presented in the various manuscripts as well as the principles illucidated during the panel discussions should provide the reader a current state-of-the-art understanding as well as clues for future directions in these important cardiovascular therapeutic classes.

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OCTOBER 27-28, 1988

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