ApoA-I Milano

*Am J Hum Genet* 37:1083–1097, 1985

**AI_{Milano}** Apoprotein Identification of the Complete Kindred and Evidence of a Dominant Genetic Transmission

Valter Gualandri,^{1} Guido Franceschini,^{2} Cesare R. Sirtori,^{2} Gemma Gianfranceschi,^{2} Giovann Battista Orsini,^{1} Antonio Cerrone,^{3} and Alessandro Menotti^{4}
Effect of Recombinant ApoA-I Milano on Coronary Atherosclerosis in Patients With Acute Coronary Syndromes
A Randomized Controlled Trial

Steven E. Nissen, MD; Taro Tsunoda, MD; E. Murat Tuzcu, MD; et al


Preliminary Communication

November 5, 2003

Effect of Recombinant ApoA-I Milano on Coronary Atherosclerosis

Editorial

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High-Density Lipoproteins as an Emerging Therapeutic Target for Atherosclerosis

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The Medicines Company Discontinues Development of MDCO-216, its Investigational Cholesterol Efflux Promoter

7 Nov 2016

— Top-line efficacy data from the MILANO-PILOT trial, which enrolled 126 patients, provide insufficient basis for further investment by the Company —

MILANO-PILOT

• Well-executed IVUS trial by world class investigators
• Three times the size of the original apoA-I Milano IVUS trial
• Unexpected regression in the placebo group
• Convincing negative results
ApoA-I Milano is very different structurally from wild-type apoA-I

- Arginine 173 replaced with cysteine leading to disulfide dimer formation
- Rapidly catabolized leading to reduced levels of HDL-C
ApoA-I Milano differs from wild-type apoA-I with regard to several functions

• Reduced generation of pre-beta HDL
Recombinant HDL infusion generates pre-beta HDL
ApoA-I Milano differs from wild-type apoA-I with regard to several functions

- Reduced generation of pre-beta HDL
- Reduced promotion of cholesterol efflux
ApoA-I Milano does not mobilize macrophage cholesterol in vivo as efficiently as wild-type apoA-I.
ApoA-I Milano differs from wild-type apoA-I with regard to several functions

- Reduced generation of pre-beta HDL
- Reduced promotion of cholesterol efflux
- Reduced activation of LCAT
ApoA-I Milano rHDL infusion suppresses the LCAT-mediated cholesterol esterification rate
Promoting cholesterol efflux and reducing cardiovascular events with apoA-I infusion?