IL-1 Blockade in Heart Disease

The intracellular sensing protein termed NLRP3 (for NACHT, LRR, and PYD domains-containing protein 3) forms a macromolecular structure called the NLRP3 inflammasome. The NLRP3 inflammasome plays a major role in inflammation, particularly in the production of interleukin-1b (IL-1b). IL-1b is the most studied of the IL-1 family of cytokines, including 11 members among which IL-1a and IL-18. Dr. Abbate will summarize pre-clinical and clinical findings supporting the key pathogenetic role of the NLRP3 inflammasome and IL-1 cytokines in the formation, progression and complications of atherosclerosis, in ischemic (acute myocardial infarction, AMI), and non-ischemic injury to the myocardium (myocarditis) and the progression to heart failure (HF). He will also review the clinically available IL-1 inhibitors, although not currently approved for a cardiovascular indication, and discuss other IL-1 inhibitors, not currently approved, as well as oral NLRP3 inflammasome inhibitors currently in clinical development. There is overwhelming evidence linking the NLRP3 inflammasome and the IL-1 cytokines with the pathogenesis of cardiovascular diseases. The future will likely include targeted inhibitors to block the IL-1 isoforms, and possibly oral NLRP3 inflammasome inhibitors, across a wide spectrum of cardiovascular diseases.