

## Professor Kees Hovingh

### BIOGRAPHY



Department of  
Vascular Medicine,  
Academic Medical  
Center, Amsterdam, The  
Netherlands

**G Kees Hovingh** (1974) received his medical degree at the University of Groningen in 2000, his PhD in 2005 and his MBA in 2016. Hovingh is an internist and vascular medicine specialist at the Department of Vascular Medicine at the Academic Medical Center (AMC) of the University of Amsterdam, the Netherlands and visiting professor at Imperial College in London, UK. Hovingh is co-chair of the department of internal medicine at the AMC and in his role as head of the clinical trial unit involved in a large number of clinical trials, mainly focused on novel therapies to combat (the consequences of) dyslipidemia. Hovingh gained his interest in genetic lipidology via research conducted at the AMC, and he co-authored over 200 publications (Hirsch factor: 48). Through this research, Dr Hovingh has identified mutations in a large number of pivotal genes in lipid metabolism in patients with extreme dyslipidemia phenotypes. Overall aim of the unraveling of the molecular pathology in patients is to identify novel and innovative therapeutic pathways to reduce the burden of dyslipidemia and cardiovascular disease.

### ABSTRACT

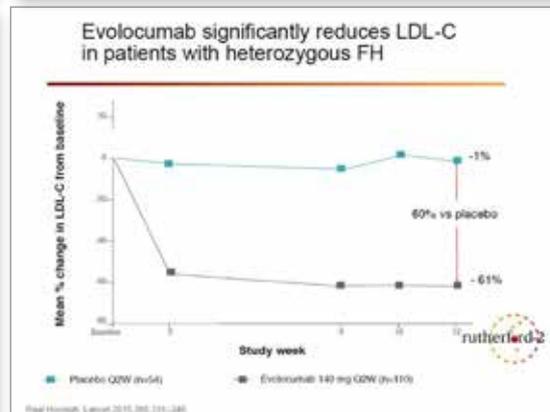
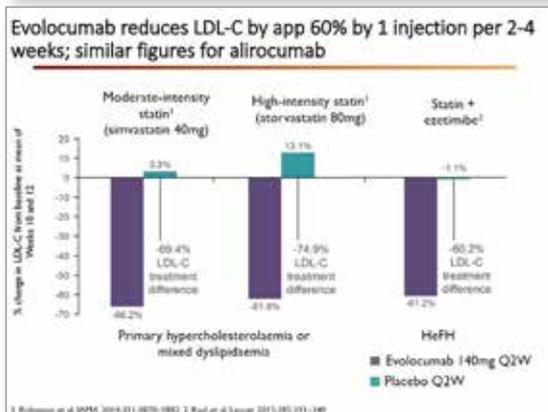
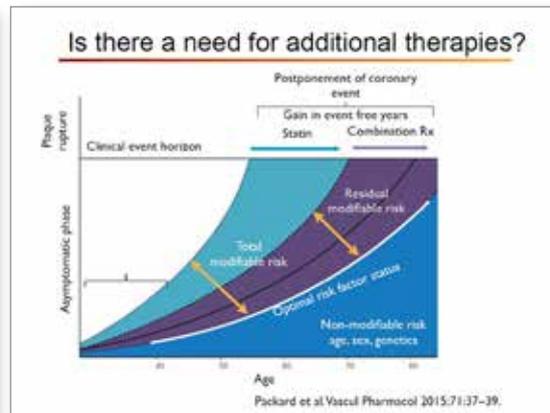
#### **PCSK9 inhibition across a wide spectrum of patients: For whom is it efficacious?**

Despite statin and/or ezetimibe treatment, many patients with heterozygous familial hypercholesterolemia, statin-intolerance or ASCVD do not reach their guideline recommended low-density lipoprotein cholesterol (LDL-C) target level. The discovery of proteins that regulate the activity of the LDL receptor (LDLR) at a post-translational level has been a major breakthrough and formed the basis for the development of novel cholesterol-lowering drugs. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a key modulator of LDL metabolism by virtue of its effect on LDLR endocytosis and degradation. Genetic studies have consistently shown that in loss-of-function PCSK9 mutations not only result in hypocholesterolemia, but also are causing relative protection against CVD. In recent years a large number of clinical trials have shown that targeting plasma PCSK9 does result in LDL-C lowering and as such, PCSK9 inhibition has become the most promising drug development success after the discovery of statins. The monoclonal antibodies against PCSK9 (evolocumab, alirocumab and bococuzimab) have been investigated in different patient categories and demonstrated robust efficacy as well as excellent safety and tolerability. Phase III trials of alirocumab and evolocumab have both shown a reduction of CVD risk. In this lecture, Kees Hovingh will briefly highlight the patient categories that have been studied and elaborate in the clinical relevance of the findings in these studies.

### Milestones on the roadmap towards acceptance of the LDL-C hypothesis

Anitschkow, the cholesterol-fed rabbit model	1913
Muller, familial hypercholesterolemia, xanthomatosis	1928
Gotman, lipoproteins in plasma correlate with CHD risk	1949
Framingham Study, CHD risk is highest in groups with highest blood cholesterol levels	1961
Nobel Prize to Konrad Bloch for elucidating cholesterol biosynthesis pathway	1964
Goldstein and Brown, the LDL receptor and regulation of cholesterol and lipoprotein metabolism	1974
Endo, discovery of the first effective statin drug (statins not marketed until 1987)	1976
Merck, discovery of mevastatin (lovastatin), later to become the first statin to reach the market	1988
Innerarity, discovery of ApoB implication in FH	1989
The statin era: (45) showing that treatment with simvastatin reduces coronary heart disease mortality	1994
Abifadel, discovery of PCSK9 implication in FH	2003
Improvis-II, adding Ezetimibe: beneficial effect on CVD	2010
PCSK9i ab outcome trial FOURIER: effect on CVD	2017

A CENTURY



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