I.R.C.C.S. Ospedale Galeazzi - Sant'Ambrogio
Gruppo San Donato

Fondazione Italiana per il cuore

WORLD HEART FEDERATION

Tavola Rotonda

La malattia cardiovascolare nella persona con diabete in Italia

Milano, 27 Marzo 2023 – ore 14.00 – 16.30

C/O EDRA SPA, Centro Leoni B, Via Spadolini n. 7, Milano

Aterosclerosi coronarica ed impatto dei nuovi farmaci ipolipemizzanti nel paziente diabetico

Prof. Daniele Andreini, MD, PhD, FESC, FSCCT

Responsabile UOC Cardiologia Universitaria ed Imaging Cardiaco, IRCCS Galeazzi Sant'Ambrogio, University of Milan.

I.R.C.C.S. Ospedale Galeazzi - Sant'Ambrogio
Gruppo San Donato

ESC GuideLines

ESC European Society of Cardiology
European Heart Journal (2019) 00, 1–71
doi:10.1093/eurheartj/ehz425

ESC GUIDELINES

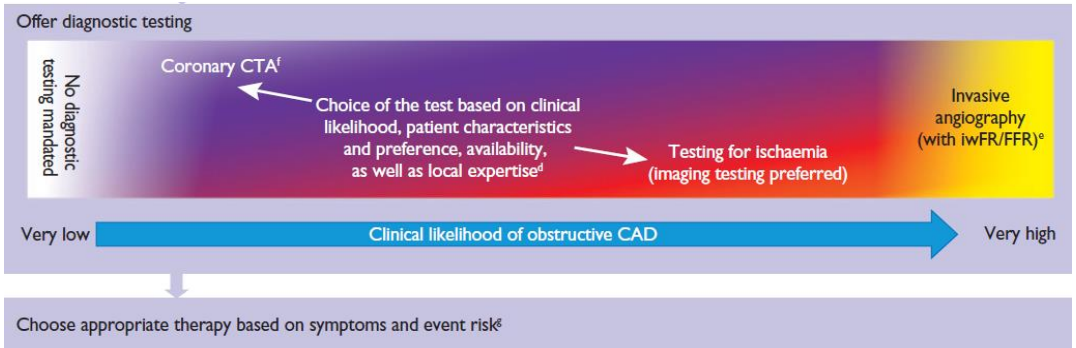
2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

New major recommendations in 2019

Basic testing, diagnostics, and risk assessment

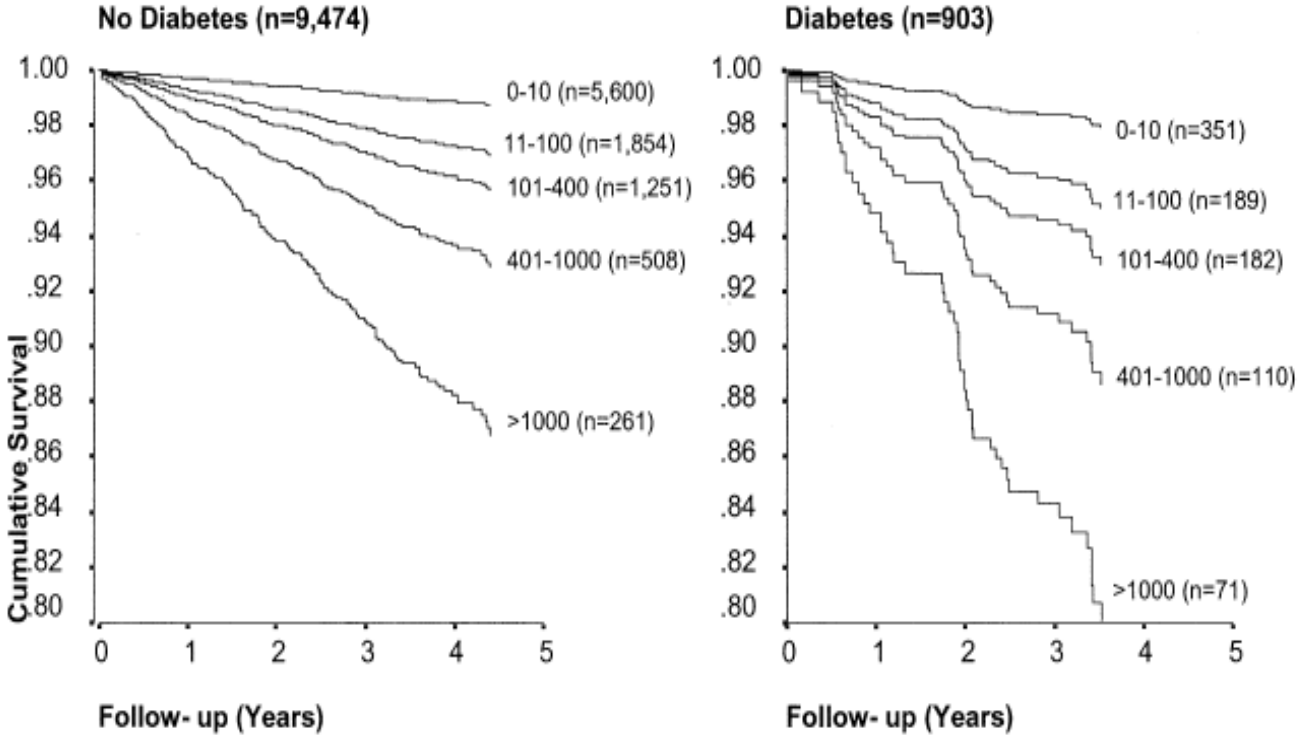
Non-invasive functional imaging for myocardial ischaemia or coronary CTA is recommended as the initial test for diagnosing CAD in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone.	I



I.R.C.C.S. Ospedale Galeazzi - Sant'Ambrogio
Gruppo San Donato

EHJ 2019

JACC Vol. 43, No. 9, 2004
May 5, 2004:1663–9



Andreini *et al. Cardiovascular Diabetology* 2010, **9**:80
http://www.cardiab.com/content/9/1/80

CARDIO VASCULAR DIABETOLOGY

ORIGINAL INVESTIGATION Open Access

Comparison of the diagnostic performance of 64-slice computed tomography coronary angiography in diabetic and non-diabetic patients with suspected coronary artery disease

Daniele Andreini[1*], Gianluca Pontone[1], Antonio L Bartorelli[1], Piergiuseppe Agostoni[1], Saima Mushtaq[1], Laura Antonioli[1], Sarah Cortinovis[1], Mauro Canestrari[2], Andrea Annoni[1], Giovanni Ballerini[1], Cesare Fiorentini[1], Mauro Pepi[1]

-100 paz diabetici (86 tipo 2)

-Sensibilità per stenosi >50%: 94%

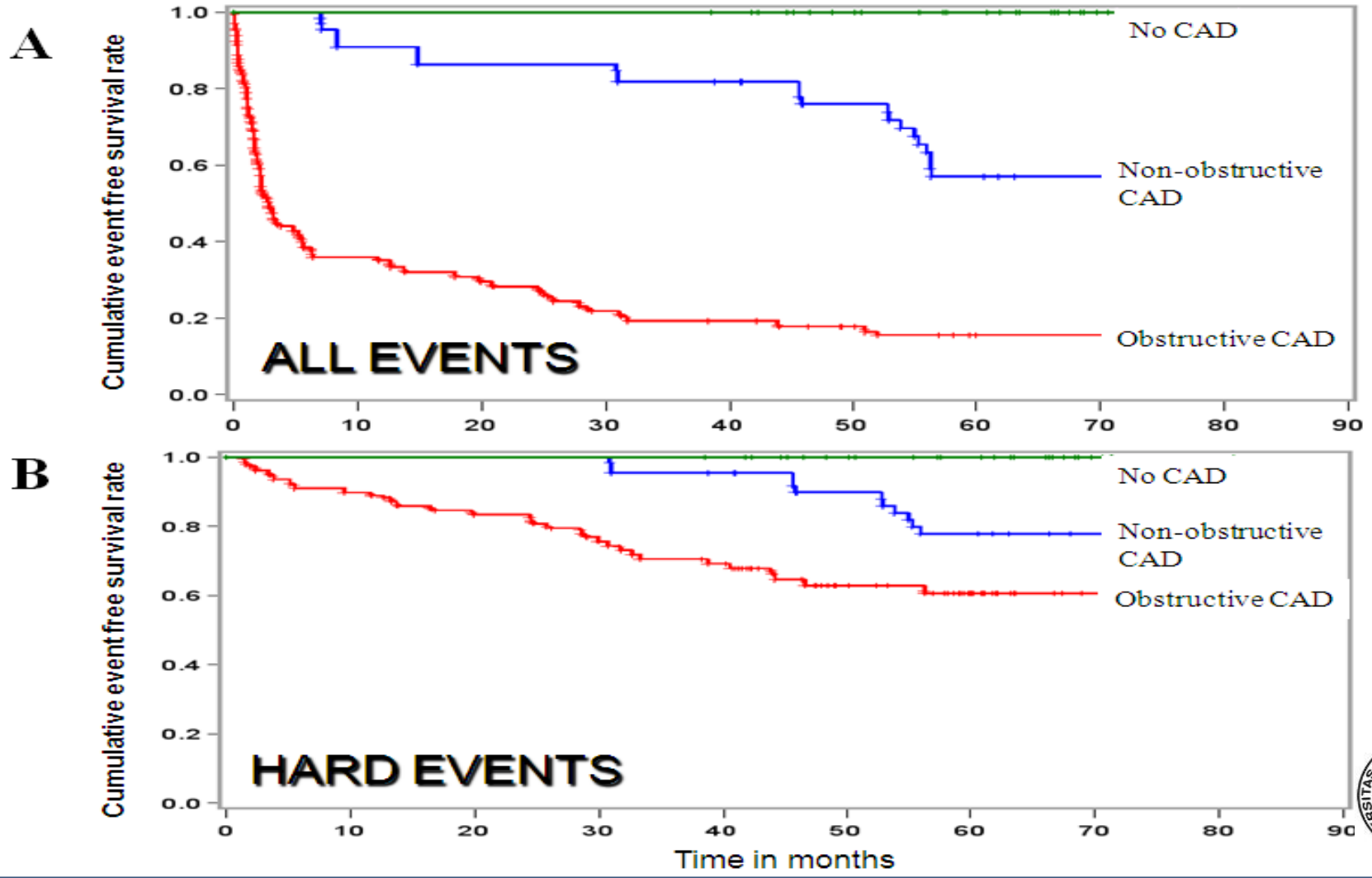
Diabetes Care Symposium
ORIGINAL ARTICLE

Prognostic Value of Multidetector Computed Tomography Coronary Angiography in Diabetes

Excellent long-term prognosis in patients with normal coronary arteries

DANIELE ANDREINI, MD[1,2]
GIANLUCA PONTONE, MD[1]
SAIMA MUSHTAQ, MD[1]
ERIKA BERTELLA, MD[1]
EDOARDO CONTE, MD[1]
ANDREA BAGGIANO, MD[1]
FABRIZIO VEGLIA, PHD[1]
PIERGIUSEPPE AGOSTONI, MD, PHD[1,2]
ANDREA ANNONI, MD[1]
ALBERTO FORMENTI, MD[1]
PIERO MONTORSI, MD[1,2]
GIOVANNI BALLERINI, MD[1]
ANTONIO L. BARTORELLI, MD[1,2]
CESARE FIORENTINI, MD[1,2]
MAURO PEPI, MD[1]

Of the 429 patients enrolled, 24 were excluded from the analysis because of the MDCT data set was judged uninterpretable. Of the remaining 405 patients, **clinical follow-up (mean 62 ± 9 months, up to 72 months)** was obtained for 390 (98%; diet in 40 patients, oral antidiabetic medication in 281 pts, insulin in 69 pts).


A
Cumulative event free survival rate
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
60
70
80
90
No CAD
Non-obstructive CAD
Obstructive CAD
ALL EVENTS
B
Cumulative event free survival rate
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
60
70
80
90
No CAD
Non-obstructive CAD
Obstructive CAD
HARD EVENTS
Time in months

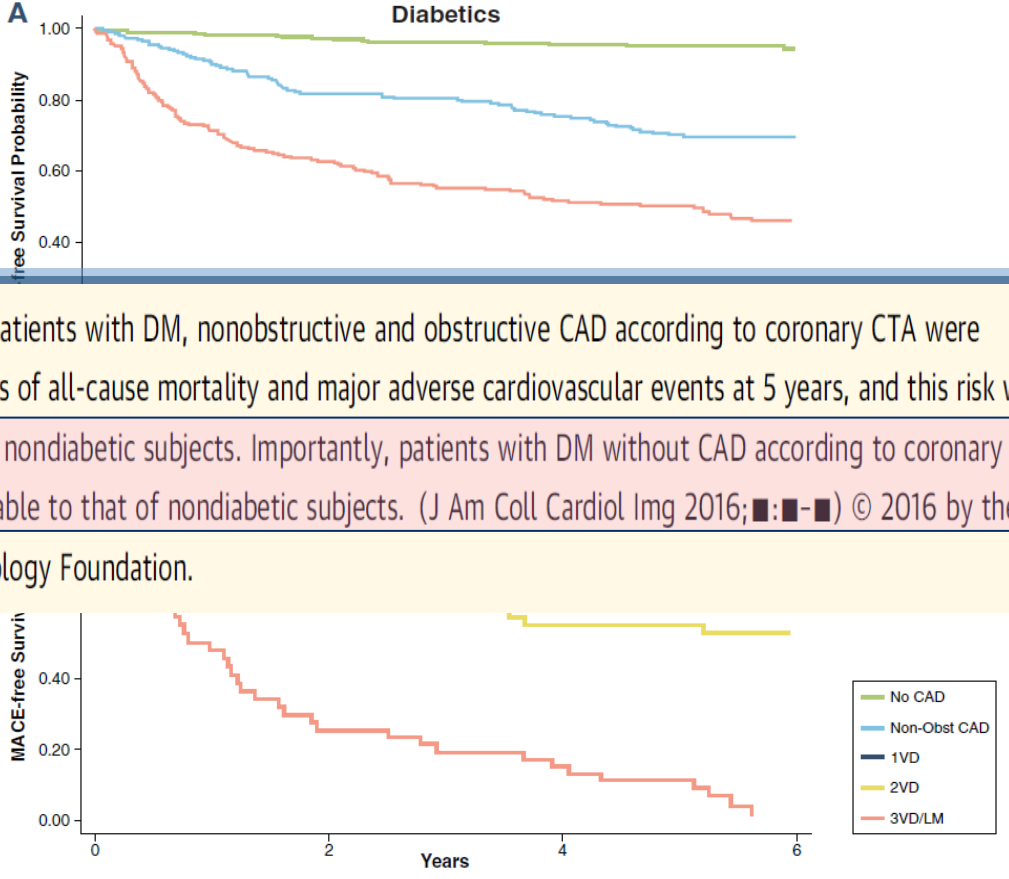
JACC: CARDIOVASCULAR IMAGING
© 2016 BY THE AMERICAN COLLEGE OF
PUBLISHED BY ELSEVIER

NO. ■, 2016
-878X/$36.00
g.2015.12.027

Long-Term P
Coronary CT
Patients With

Philipp Blanke, MD,[a] Christopher
Jeanette Soon, MBBS,[a] Chesnal A
Matthew J. Budoff, MD,[e] Tracy O
Kavitha Ch
Todd C. Vil
Philipp A.
Gilbert Raff
James Min,
rman, MD,[c]
ei, MD,[h]
ow, MD,[w]

FIGURE 4 Risk-Adjusted Kaplan-Meier Curve for Event-Free Survival Stratified According to CAD



CONCLUSIONS Among patients with DM, nonobstructive and obstructive CAD according to coronary CTA were associated with higher rates of all-cause mortality and major adverse cardiovascular events at 5 years, and this risk was significantly higher than in nondiabetic subjects. Importantly, patients with DM without CAD according to coronary CTA were at a risk comparable to that of nondiabetic subjects. (J Am Coll Cardiol Img 2016;■:■-■) © 2016 by the American College of Cardiology Foundation.

I.R.C.C.S. Ospedale Galeazzi - Sant'Ambrogio
Gruppo San Donato

Contents lists available at ScienceDirect

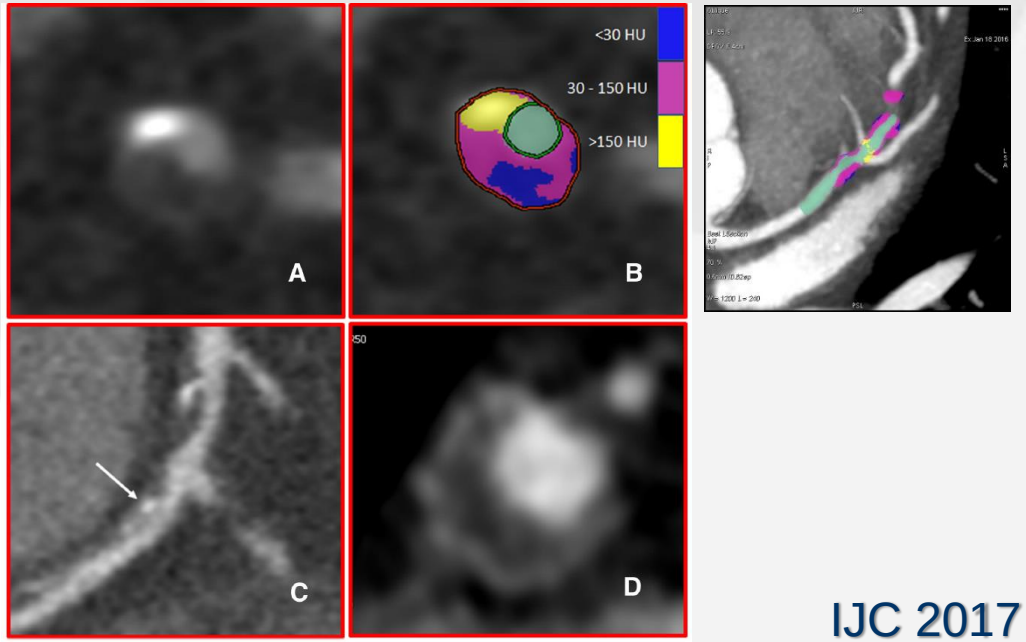
International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Review

Role of new imaging modalities in pursuit of the vulnerable plaque and the vulnerable patient

Paolo Raggi [a,b,*], Gianluca Pontone [c,d], Daniele Andreini [c,e]



I.R.C.C.S. Ospedale Galeazzi - Sant'Ambrogio
Gruppo San Donato

IJC 2017

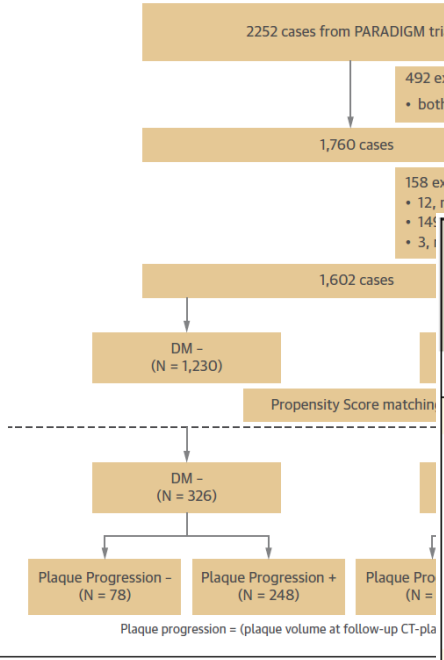
JACC: CARDIOVASCULAR IMAGING
VOL. ■, NO. ■, 2018
© 2018 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

Natural History of Diabetic Coronary Athe… ve Meas… ary Com… iography

Results… n of Atherosclerotic Plaque… phic Angiography Imagin…

Ung Kim, M…
Philipp Blar…
Daniele And…
Byoung Kw…
Hugo Marqu…
Peter H. Sto…
James K. Mi…
…D [a,c] Michael Shao, BS [a]
…, [f]
…D, PHD, [h]
…MD, [i]
… Samady, MD, [q]
… Bax, MD, PHD, [v]

FIGURE 1 Flow Chart of the Study Population



…iography; DM = diabetes mellitus; PARADIGM = Progression …raphy Imaging.

TABLE 4 Independent Risk Factors for Plaque Progression in the Nonmatched Cohort (N = 1,602) and in Patients With DM (N = 326) on Multivariate Logistic Regression Analysis

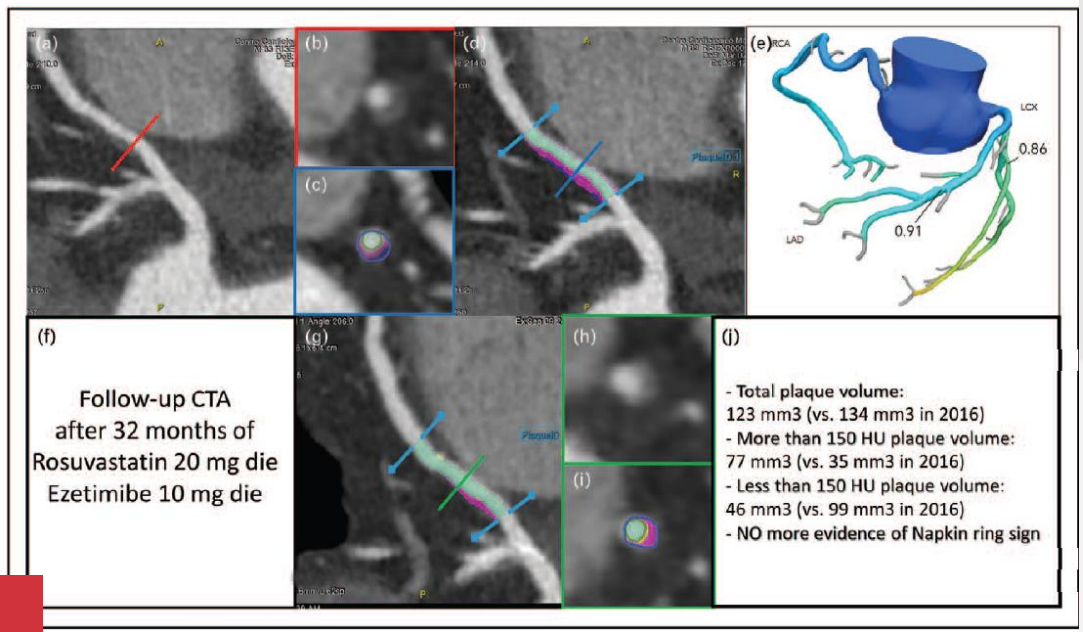
	OR	95% CI	p Value
Nonmatched cohort			
Age ≥55 yrs	1.418	1.080-1.862	0.012
DM	1.526	1.100-2.118	0.011
Hypertension	1.302	1.011-1.677	0.041
Statin treatment at baseline	0.716	0.555-0.923	0.010
Mean plaque burden ≥75% at baseline	3.151	1.988-4.995	<0.001
DM patients			
Male	1.485	1.003-2.199	0.048
Mean plaque burden ≥75% at baseline	3.121	1.701-5.725	<0.001

I.R.C.C.S. Ospedale Galeazzi - Sant'Ambrogio
Gruppo San Donato

Coronary plaque features on CTA can identify patients at increased risk of cardiovascular events

Daniele Andreini[a,b], Edoardo Conte[a,c], and Patrick W. Serruys[d,e]

56 YO
Type 2 DM



Glycemic control is independently associated with rapid progression of coronary atherosclerosis in the absence of a baseline coronary plac ve case–control study istry

Ki-Bum Won[1,2,3], Byoung Kwor Min Sung[2,3], Edoardo Conte[8], Daniele Andreini[9], Gianluca Po [12], Filippo Cademartiri[13], Erica Maffei[13], Hugo Marques[1 Sang-Eun Lee[17], Sanghoon Shin[17], Jung Hyun C yan[21], Daniel S. Berman[22], Jagat Narula[23], Leslee J. Shaw[2

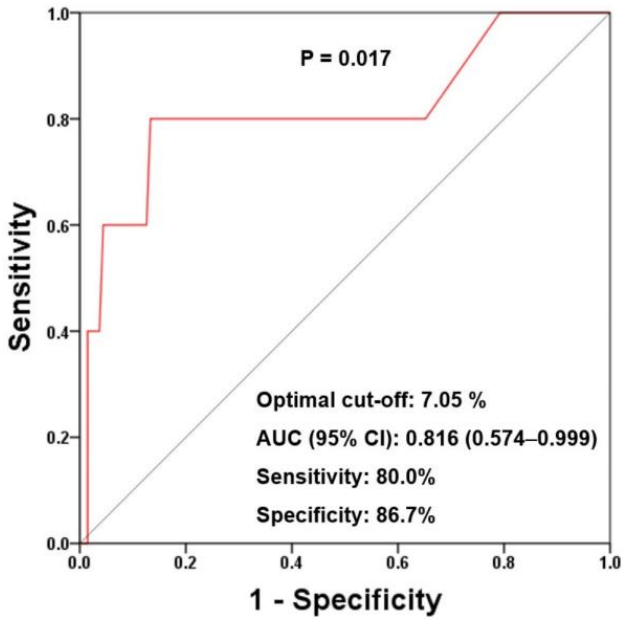


Fig. 1 Receiver operating characteristic curve with respect to the serum hemoglobin A1c level for predicting RPP. RPP: rapid plaque progression
RPP: rapid plaque progression

I.R.C.C.S. Ospedale Galeazzi - Sant'Ambrogio
Gruppo San Donato

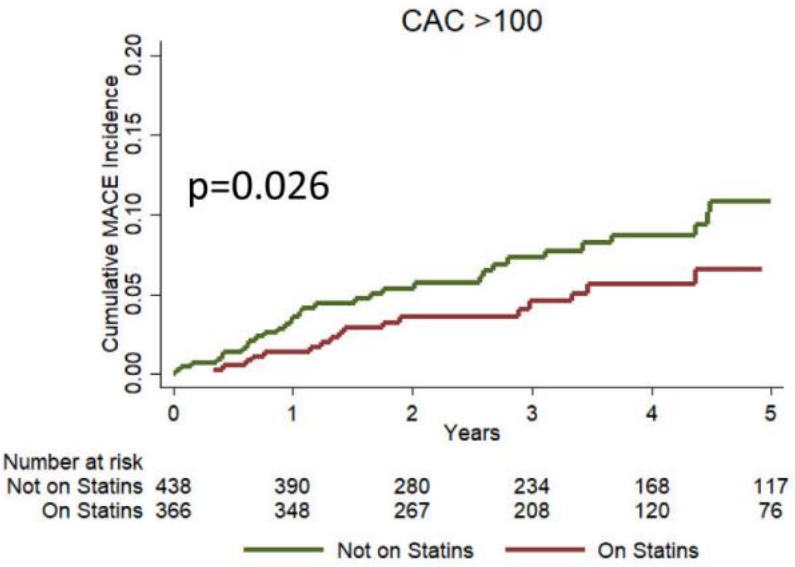
Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: www.elsevier.com/locate/jdiacomp

Extent of subclinical atherosclerosis on coronary computed tomography and impact of statins in patients with diabetes without known coronary artery disease: Results from CONFIRM registry☆

Kashif Shaikh [a,b,*], Arslan Ahı… [f], Rine Nakanishi [a], Venkata All… [c], Erica Maffei [i], Fay Y. Lin [j], Aiz… Gudrun Feuchtner [m], Hugo M… [p], Philipp A. Kaufmann [q,r], Pedr… [t], Hyuk-Jae Chang [j], Ronen Rub… Stephen Acenbach [x], Mouaz H… Tracy Q. Callister [aa], Matthew…



I.R.C.C.S. Ospedale Galeazzi - Sant'Ambrogio
Gruppo San Donato

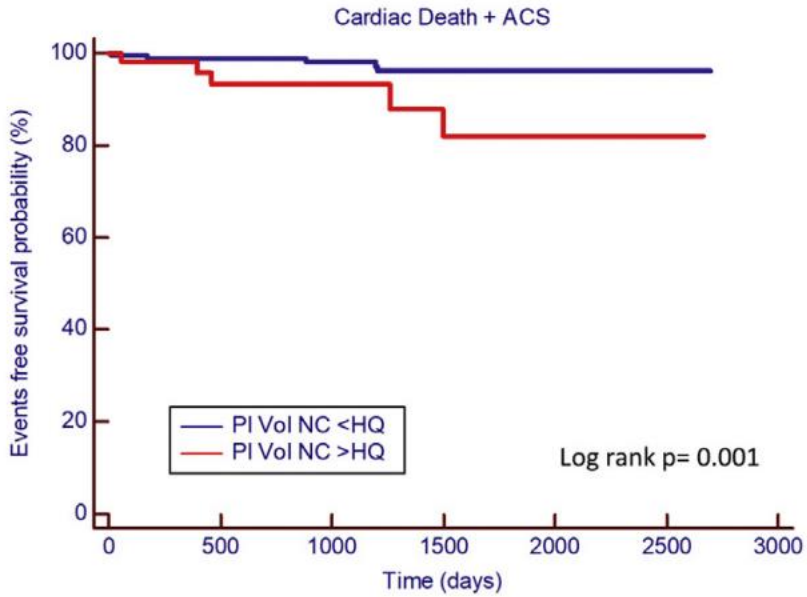
Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

Plaque assessmer … cardiac events in high ris … g-term follow-up study

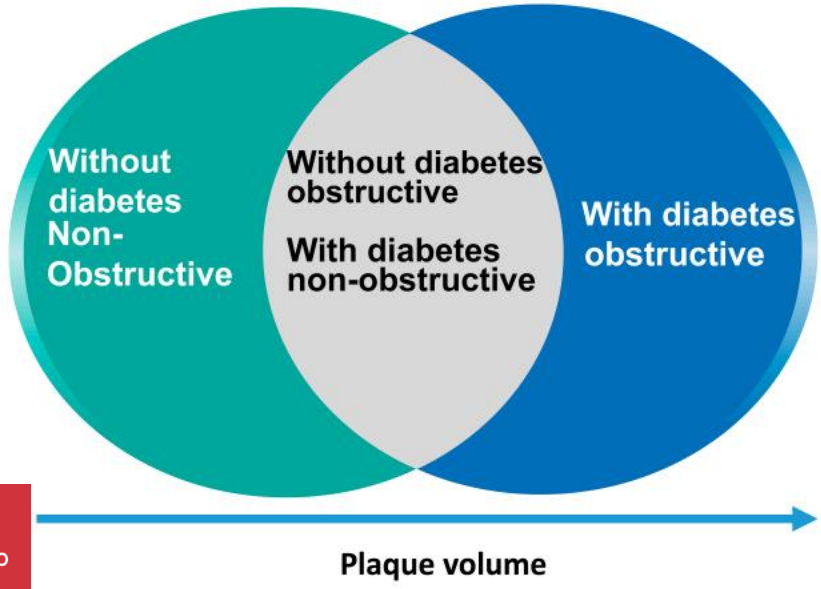
Daniele Andreini [a,b,*,1], Federica Traversari [a], … Asinelli [a], Andrea Ann … lielmo [a], Andrea Baggiano [a], El… inelli [a], Gianluca Pontone [a], A…

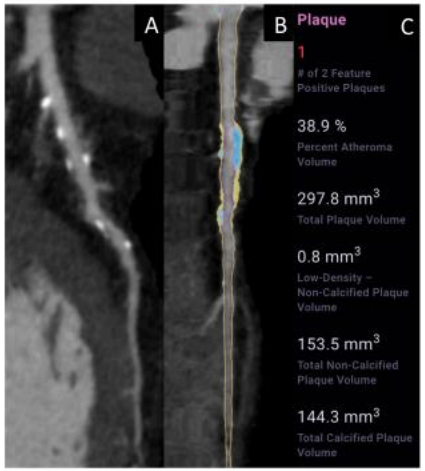


I.R.C.C.S. Ospedale Galeazzi - Sant'Ambrogio
Gruppo San Donato

Diabetes, Atherosclerosis, and Stenosis by AI

Diabetes Care 2023;46:416–424 | https://doi.org/10.2337/dc21-1663





Atherosclerosis burden in a patient with diabetes with nonobstructive stenosis.

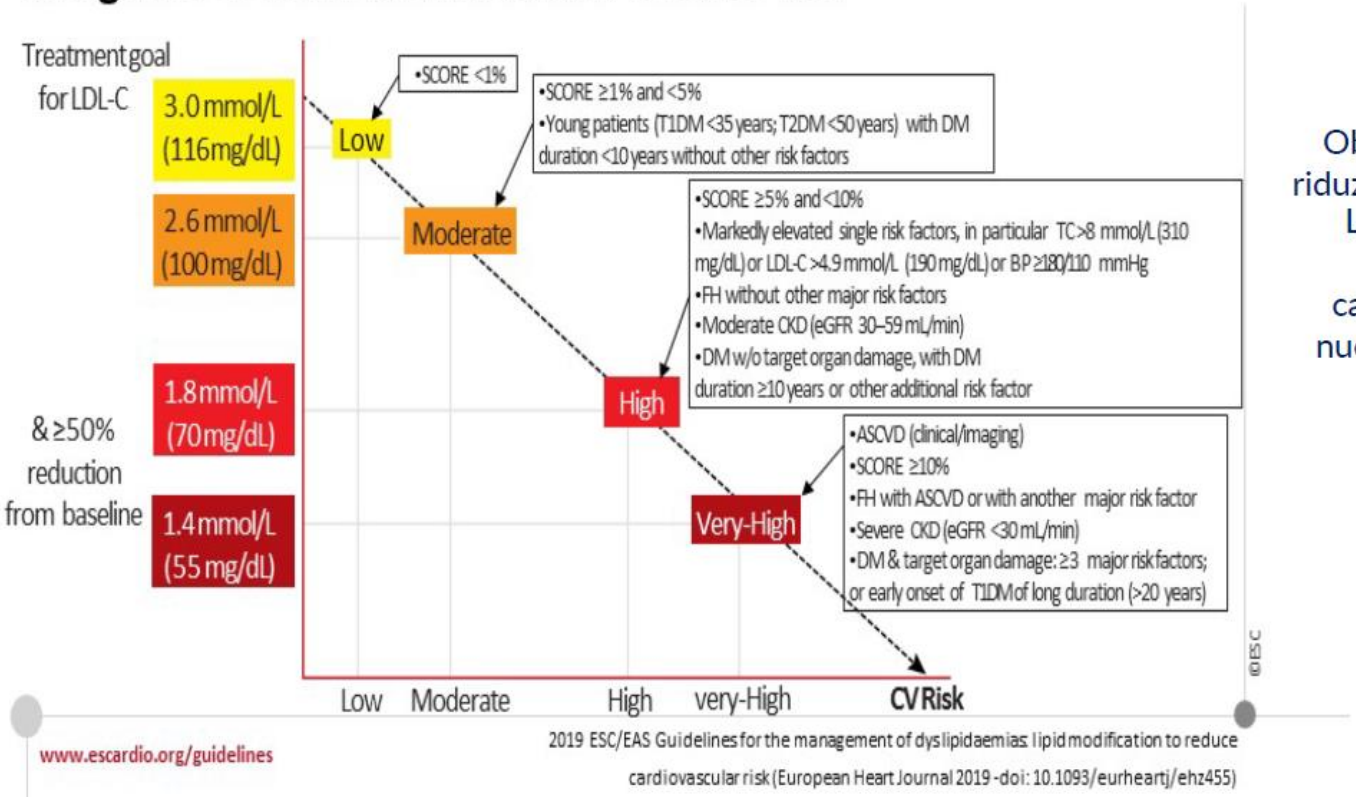
JACC: CARDIOVASCULAR IMAGING
VOL. ■, NO. ■, 2016
© 2016 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2016.01.039

EDITORIAL COMMENT

Screening CT Angiography in Asymptomatic Diabetes Mellitus?*

Daniele Andreini, MD, PhD

Central Illustration Upper panel Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk

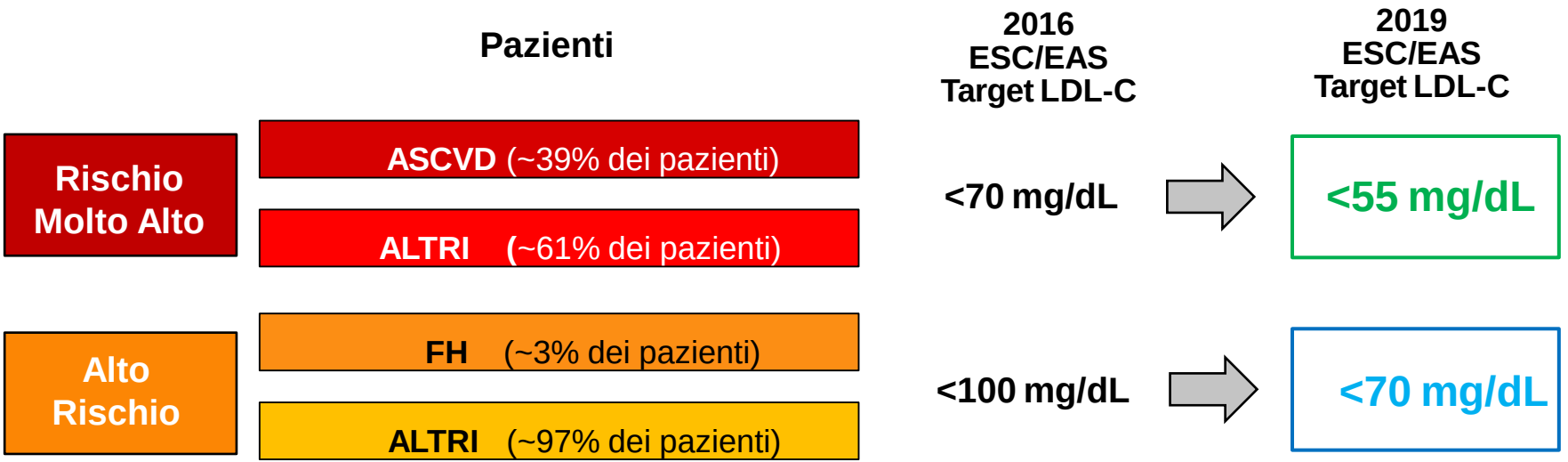


www.escardio.org/guidelines

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Obiettivi terapeutici di riduzione del colesterolo LDL in funzione della classe di rischio cardiovascolare. Nelle nuove linee guida sono stabiliti target più ambiziosi.

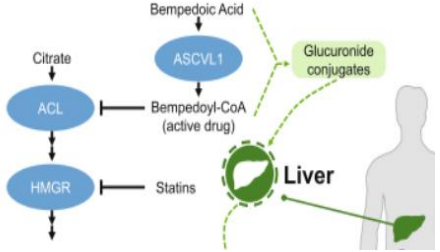
Il profilo di rischio CV determina la necessità di un controllo stringente dei livelli di LDL come sottolineato dalle nuove Linee Guida EAS/ESC



Mach F et al. Eur Heart J. 2020; 41:111-88;
Catapano A et al. Eur Heart J. 2016; 37(39):2999-3058

Role of Bempedoic Acid in Clinical Practice

Christie M. Ballantyne[1] • Harold Bays[2] • Alberico L. Catapano[3] • Anne Goldberg[4] • Kausik K. Ray[5] • Joseph J. Saseen[6]



First-in-class, Oral, Once-daily LDL-C Lowering Therapy

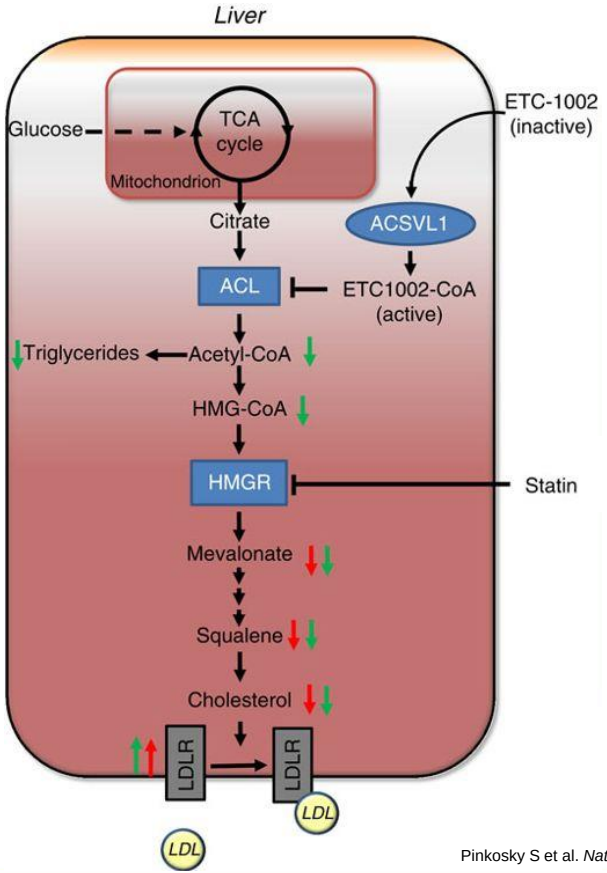
Bempedoic acid and bempedoic acid/ezetimibe FDC are indicated for patients with hypercholesterolaemia or mixed dyslipidaemia who are not at LDL-C goal with a maximally tolerated dose of statin and/or ezetimibe[1–2]

- **Bempedoic acid (180 mg) and it's fixed-dose combination with ezetimibe (180 mg bempedoic acid/10 mg ezetimibe FDC) are novel, oral options, which can be added to existing, oral LLTs* to deliver the additional LDL-C reductions that uncontrolled patients need**
- **Oral, once-daily bempedoic acid and bempedoic acid/ezetimibe FDC can be taken with or without food, at a time that suits the patient[1,2]**
- **Bempedoic acid, as well as its active metabolite and glucuronide forms are not metabolised by and do not inhibit or induce cytochrome P450 enzymes[1,2]**
- **Add bempedoic acid and bempedoic acid/ezetimibe FDC to current oral LLTs to help uncontrolled patients who are at high- or very-high-CV risk to achieve their LDL-C goals**

The Unique Mechanism of Action of Bempedoic Acid is Complementary, yet Distinct from Statins and Other LLTs

- **Activated primarily in the liver, bempedoic acid inhibits the ACL (ATP citrato liasi) enzyme in the well-known cholesterol synthesis pathway, upstream of the statin target (HMG-CoA-reduttasi)**

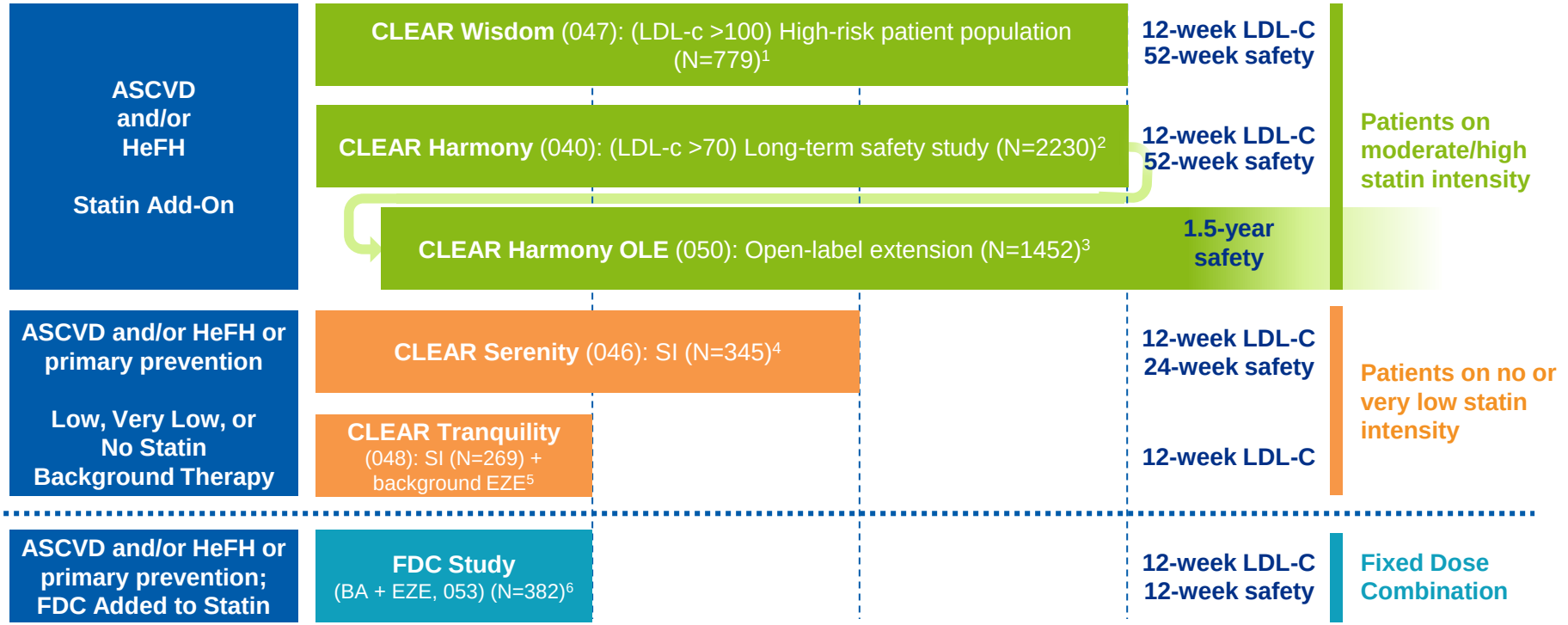
- **Upregulation of the LDL receptor results in an increased uptake and removal of LDL particles by the liver**



Aumento dell'espressione dei recettori delle LDL sulla superficie dell'epatocita che determina un aumento dell'assorbimento e della rimozione delle particelle LDL da parte del fegato

Pinkosky S et al. *Nat Commun*. 2016;7:13457. doi: 10.1038/ncomms1345

Bempedoic Acid Was Evaluated in a Robust Clinical Trial Program with a Broad Range of Patients: CLEAR (Cholesterol lowering via bempedoic acid, an ACL-Inhibiting regimen)



ASCVD = atherosclerotic cardiovascular disease; BA = bempedoic acid; EZE = ezetimibe; HeFH = heterozygous familial hypercholesterolemia; LDL-C = low-density lipoprotein cholesterol; OLE = open-label extension; SI = statin intolerant

1.Goldberg AC et al. JAMA. 2019;322(18):1780-1788. doi:10.1001/jama.2019.16585; **2.** Ray KK, et al. *N Engl J Med*. 2019;380:1022-32; **3.** ClinicalTrials.gov identifier NCT03067441; **4.** Laufs U, et al. *J Am Heart Assoc*. 2019;8:e011662; **5.** Ballantyne CM, et al. *Atherosclerosis*. 2018;277:195-2036. **6.** Ballantyne CM et al. *Eur J Prev Cardiol*. 2020;27(6):593-603.

Bempedoic Acid is a New Solution for Uncontrolled LDL-C Patients at High and Very High Risk After Optimized Oral Lipid Lowering Therapies

From 17 to 28% reduction in LDL-C with bempedoic acid

Significant reductions in LDL-C vs placebo on top of maximally tolerated statins ± other oral LLTs

38% reduction in LDL-C with bempedoic acid/ezetimibe FDC

Efficacy & Safety

hsCRP; Glicemia

Additional treatment with bempedoic acid does not lead to an overall increase of side effects vs placebo on top of existing LLTs

Combined safety analysis in more than 3,600 patients

Bempedoic acid and bempedoic acid/ezetimibe were well tolerated

A Combined Safety Analysis in More Than 3,600 Patients Confirmed that Bempedoic Acid is Well Tolerated

Treatment-Emergent AEs	Bempedoic Acid N=2424, % (n)	Placebo N=1197, % (n)	*p*
Muscular weakness	0.5 (13)	0.6 (7)	0.82
New-onset diabetes/hyperglycemia	4.0 (96)	5.6 (67)	0.03
Blood uric acid increased	2.1 (51)	0.5 (6)	< 0.001
Hyperuricemia	1.7 (40)	0.6 (7)	0.007
Gout	1.4 (33)	0.4 (5)	0.008
Blood creatinine increased	0.8 (19)	0.3 (4)	0.12
Glomerular filtration rate decreased	0.7 (16)	<0.1 (1)	0.02
Hepatic enzyme elevation	2.8 (67)	1.3 (15)	0.004
> 3 times the upper reference limit	0.7 (18)	0.3 (3)	0.10
> 5 times the upper reference limit	0.2 (6)	0.2 (2)	> 0.99
Neurocognitive disorderse	0.7 (16)	0.8 (9)	0.83

AE – adverse event; LLTs = lipid lowering therapies.

Adverse events of special interest

- The incidences of myalgia and muscle weakness were similar between treatment groups in patients receiving background high-intensity statin therapy
- Modest changes in creatinine, uric acid and occurred early, were stable, and were reversible after drug discontinuation
- Gout occurred more frequently with bempedoic acid compared with placebo, although the incidence was low in both treatment groups and events occurred primarily in patients with a prior diagnosis of gout

Acido bempedoico attiva la protein-chinasi attivata da adenosina monofosfato (AMPK) e quindi potrebbe avere effetti positivi anche su glicemia e insulino-resistenza. *Norata et al.*

Banach M. et al., JAMA Cardiology, published online July 1, 2020. doi:10.1001/jamacardio.2020.2314

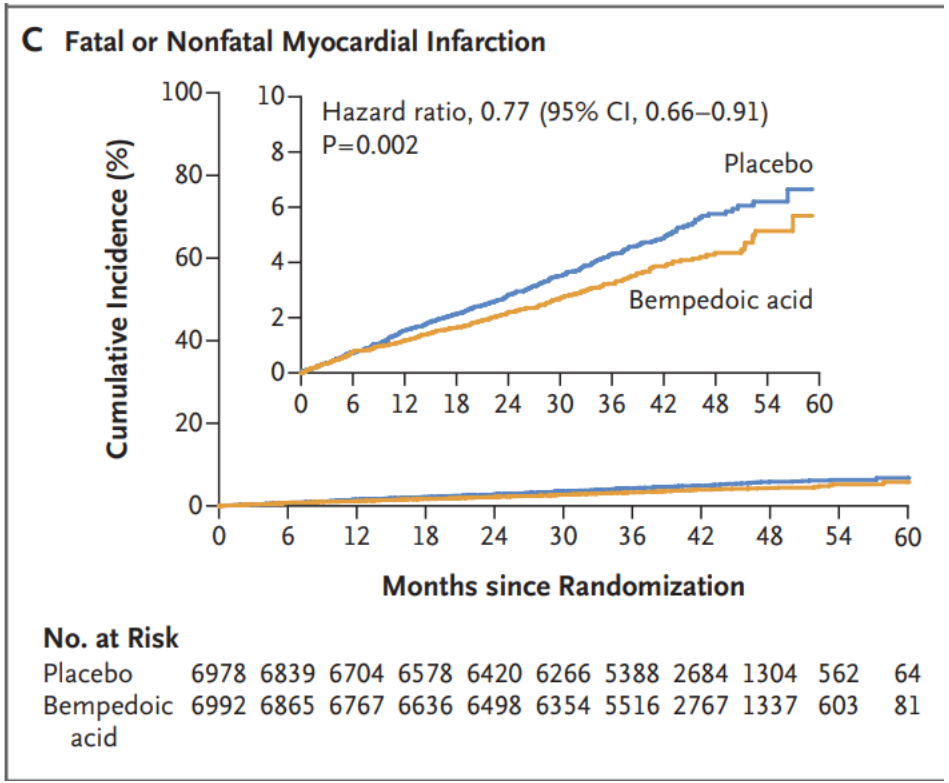
ORIGINAL ARTICLE

Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients

S.E. Nissen, A.M. Lincoff, D. Brennan, K.K. Ray, D. Mason, J.J.P. Kastelein, P.D. Thompson, P. Libby, L. Cho, J. Plutzky, H.E. Bays, P.M. Moriarty, V. Menon, D.E. Grobbee, M.J. Louie, C.-F. Chen, N. Li, L.A. Bloedon, P. Robinson, M. Horner, W.J. Sasiela, J. McCluskey, D. Davey, P. Fajardo-Campos, P. Petrovic, J. Fedacko, W. Zmuda, Y. Lukyanov, and S.J. Nicholls, for the CLEAR Outcomes Investigators*

Table 1. Demographic and Baseline Patient Characteristics in the Intention-to-Treat Population.*

Characteristic	Bempedoic Acid (N=6992)	Placebo (N=6978)
Age		
Mean — yr	65.5±9.0	65.5±8.9
Glycemic status — no. (%)		
Diabetes§	3144 (45.0)	3229 (46.3)
Inadequately controlled diabetes¶	1356 (19.4)	1369 (19.6)



New-onset diabetes in patients with prediabetes at baseline — no./total no. (%)†	569/2918 (19.5)	586/2877 (20.4)
New-onset diabetes in patients with normoglycemia at baseline — no./total no. (%)†	52/938 (5.5)	54/863 (6.3)

Daniele Andreini, MD, PhD, FESC, FSCCT

Associate Professor of Cardiovascular Disease, University of Milan, Italy

Director of University Cardiology and Cardiac Imaging, IRCCS Galeazzi Sant'Ambrogio, Milan, Italy

Scientific Advisor, OLV-Aalst CV Center

Associate Editor of the Journal of CV Computed Tomography

Section Editor (Noninvasive imaging) of the Eurointervention

Chairman of Europe Committee, Society of CV Computed Tomography

Member of GuideLines Committee, Society of CV Computed Tomography

Member of Scientific Documents Committee, European Association of CV Imaging

Member of Scientific Board, EuroPCR

Vice Chairman, Working Group on Sport Cardiology, Italian Society of Cardiology

President Elected, Sezione Lombardia, Italian Society of Cardiology

Chairman of Cardiac Imaging, Italian Society of Sport Cardiology

daniele.andreini@grupposandonato.it

daniele.andreini@unimi.it

I.R.C.C.S. Ospedale Galeazzi - Sant'Ambrogio

Gruppo San Donato