BIELLA CUORE
12-13 SETTEMBRE 2025

La terapia di associazione con acido bempedoico: quali prospettive

PL. Temporelli

Istituti Clinici Scientifici Maugeri
Divisione di Cardiologia Riabilitativa, Gattico-Veruno

Istituti Clinici Scientifici Maugeri

Fonti di finanziamento

Speakers Bureau/Honoraria: Amarin, Astra Zeneca, Menarini, Daiichi, Servier, SPA

Consulting Fees: Amarin, Daiichi, *Novo Nordisk, SPA*

Other: none

- ✓ **Was a new lipid-lowering therapy CLEARly necessary?**

Ipercolesterolemia: una lunga storia fatta non solo di statine

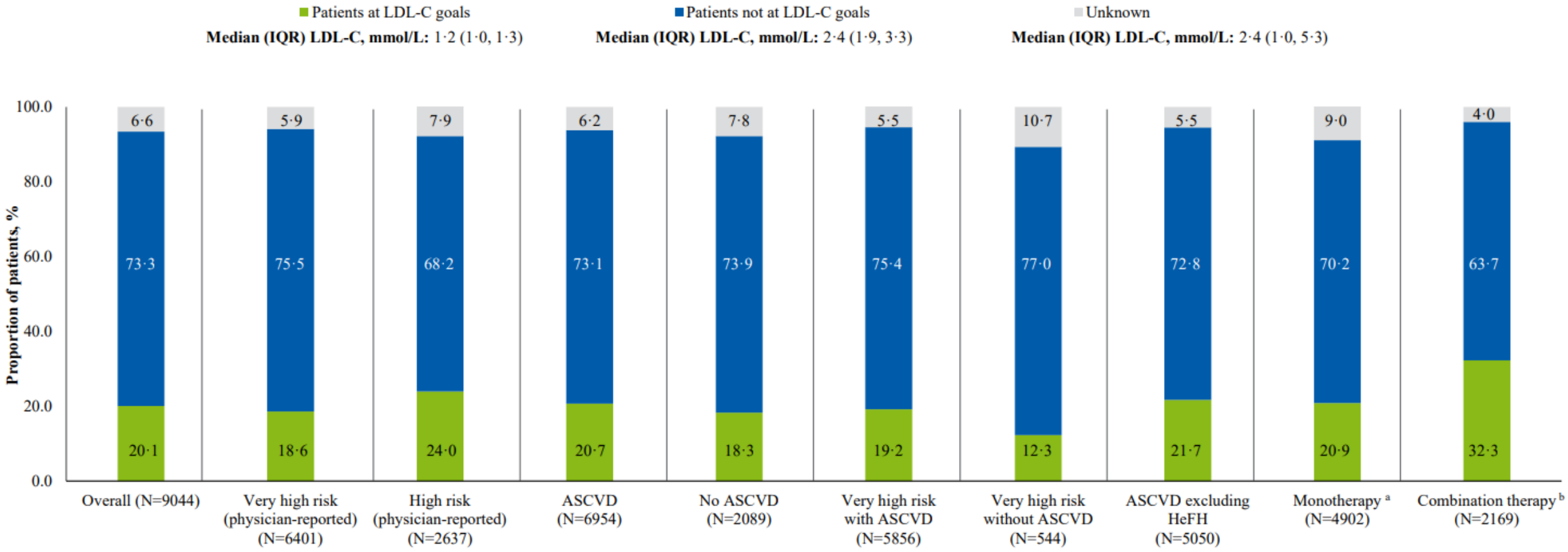
1973	Brown e Goldstein: recettore delle LDL; Endo: prima statina
1987	FDA approva lovastatina
1994	Lancet pubblica 4S
2000	Descrizione di NPC1L1
2002	FDA approva ezetimibe
2015	NEJM pubblica IMPROVE-IT
2003	Mutazioni di PCSK9 provocano ipercolesterolemia
2015	FDA approva alirocumab ed evolocumab
2017	NEJM pubblica FOURIER
2018	NEJM pubblica ODYSSEY OUTCOMES
2020	FDA approva acido bempedoico
2021	FDA approva inclisiran

Ma con tutti i farmaci che avevamo per il colesterolo c'era proprio bisogno anche di Acido Bempedoico?

Ma con tutto lo yogurt che c'è, c'era proprio bisogno di Yoplait?

Yoplait è il secondo marchio di derivati lattieri freschi più venduto al mondo

Treatment gaps in the implementation of LDL cholesterol control among high- and very high-risk patients in Europe between 2020 and 2021: the multinational observational SANTORINI study

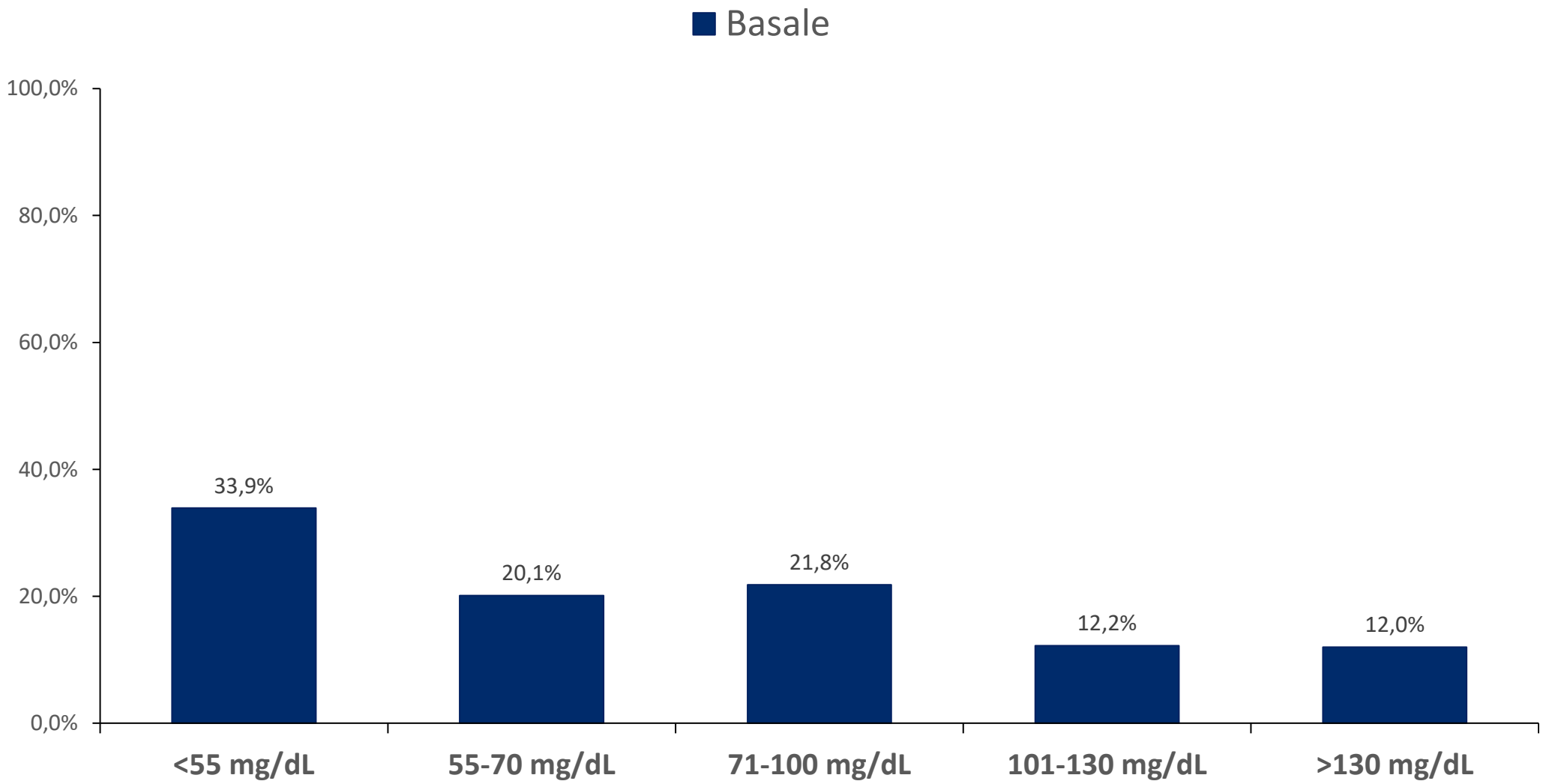


BRING•UP PREVENZIONE

Studio osservazionale, prospettico e multicentrico condotto su un ampio campione rappresentativo di centri cardiologici italiani per valutare nei pazienti con evento atero-trombotico documentato il livello di aderenza alle raccomandazioni delle linee guida

BRING•UP PREVENZIONE

Colesterolo LDL (3737 pts)



Bempedoic acid

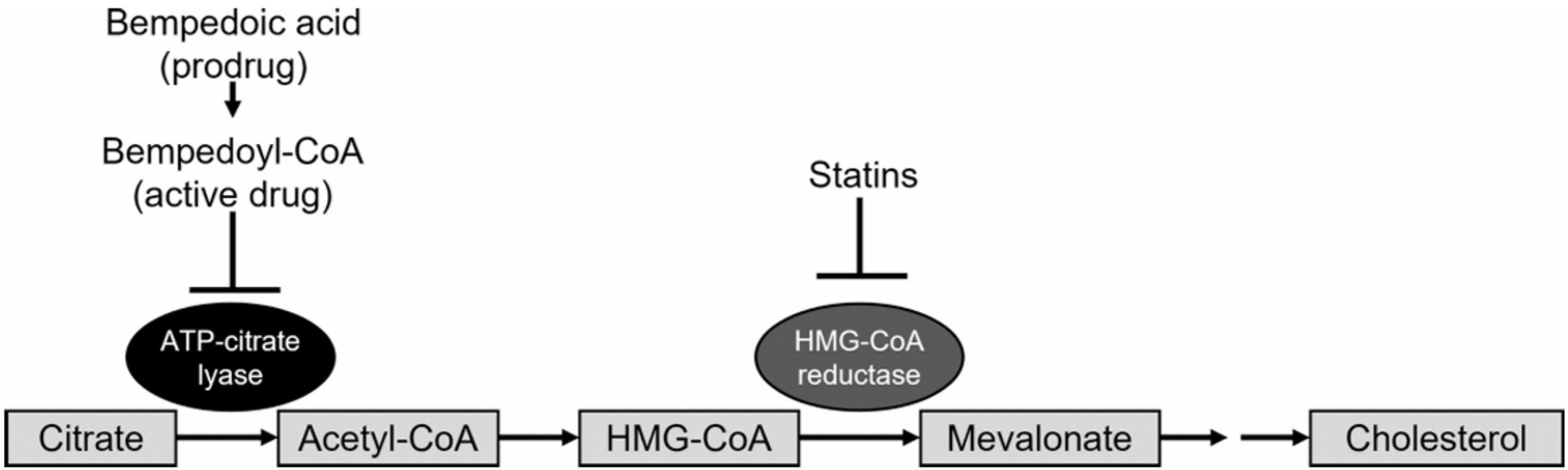
A new therapeutic option complementary to existing therapies

- «Statin therapy alone is often insufficient to achieve appropriate lowering of the low-density lipoprotein (LDL) cholesterol level.
- Hence, many patients have a cholesterol level that is not at goal for their level of perceived risk.
- A clinical need exists for the development of additional therapies that are both safe and effective in lowering the LDL cholesterol level to **complement existing therapies»**

Ray KK, et al. N Engl J Med. 2019;380:1022-32.

- ✓ **Was a new lipid-lowering therapy CLEARly necessary?**
- ✓ **Is it CLEAR how bembedoic acid works and how effective is?**

Pharmacodynamic effect of bempedoic acid and statin combinations: predictions from a dose–response model



Europ Heart J - Cardiovasc Pharmacotherapy 2021;0:1-9

Bempedoic Acid Phase 3 Clinical Trials Summary

ASCVD and/or HeFH on Statins

ASCVD and/or HeFH or Primary Prevention and Statin Intolerant

Relative reduction of LDL-C (95% CI):

CLEAR Harmony
From BL – week 12
−18.1% (−20.0, −16.1) p<0.001

CLEAR Wisdom
From BL – week 12
−17.4% (−21.0, −13.9) p<0.001

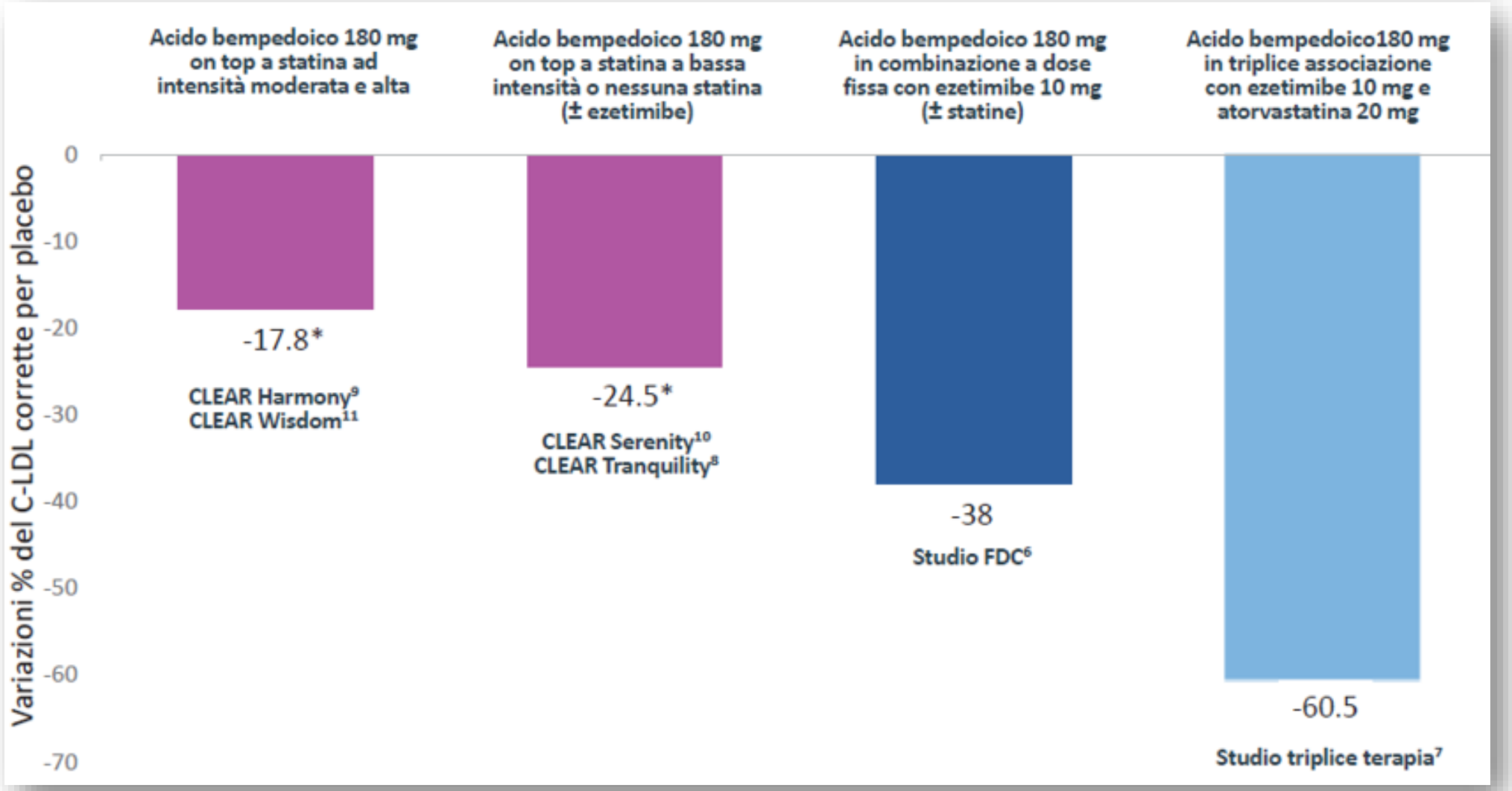
CLEAR Serenity
From BL – week 12
−21.4% (−25.1,−17.7) p<0.001

CLEAR Tranquility
From BL – week 12
−28.5% (−34.4, −22.5) p<0.001

CLEAR Outcomes
From BL – month 6
−21.1% (−20.3, −21.9) p<0.001

Ballantyne et al. Cardiovascular Drugs and Therapy 2021; Nissen SE, et al. N Engl J Med. 2023;388:1353–1364

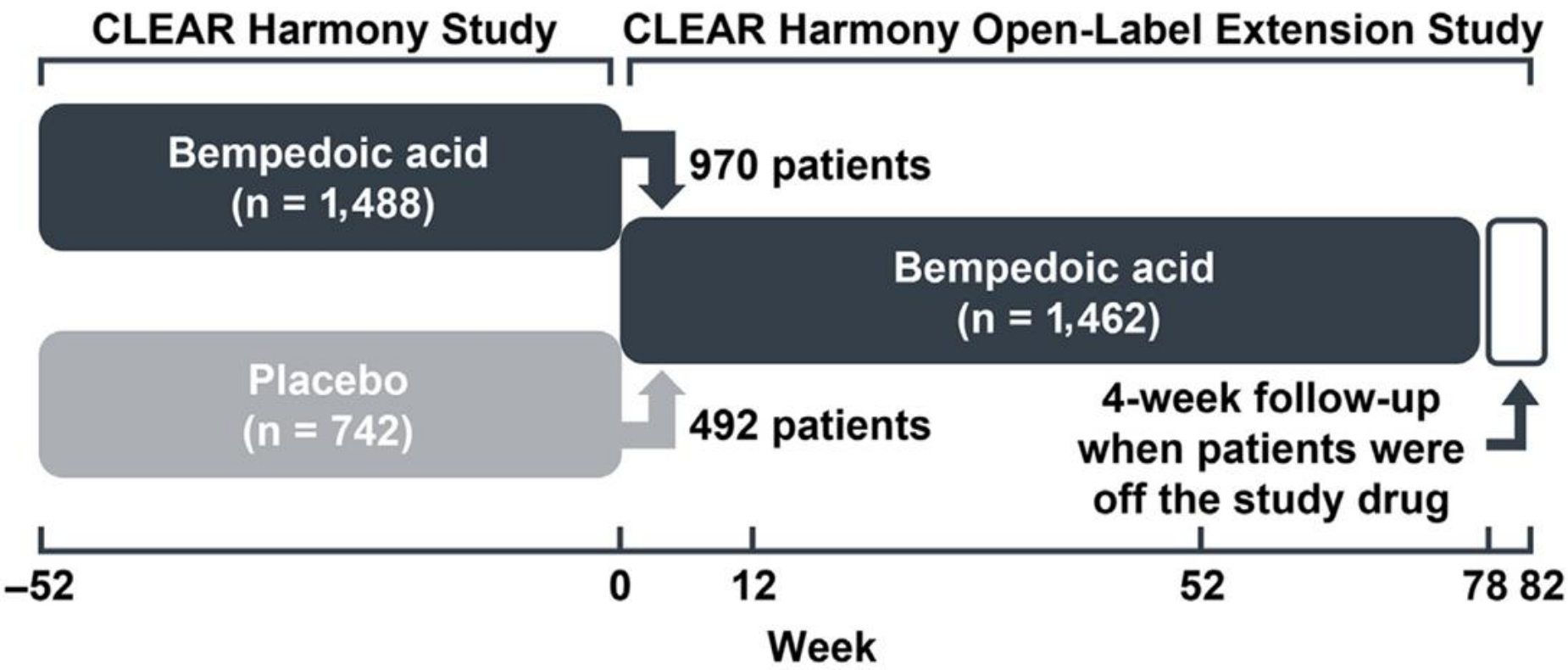
Acido bempedoico e riduzione dei livelli di C-LDL



G Ital Cardiol 2021;22(4 Suppl. 1):4S | doi 10.1714/3582.35669.

Long-Term Safety and Efficacy of Bempedoic Acid in Patients With Atherosclerotic Cardiovascular Disease and/or Heterozygous Familial Hypercholesterolemia

(from the CLEAR Harmony Open-Label Extension Study)



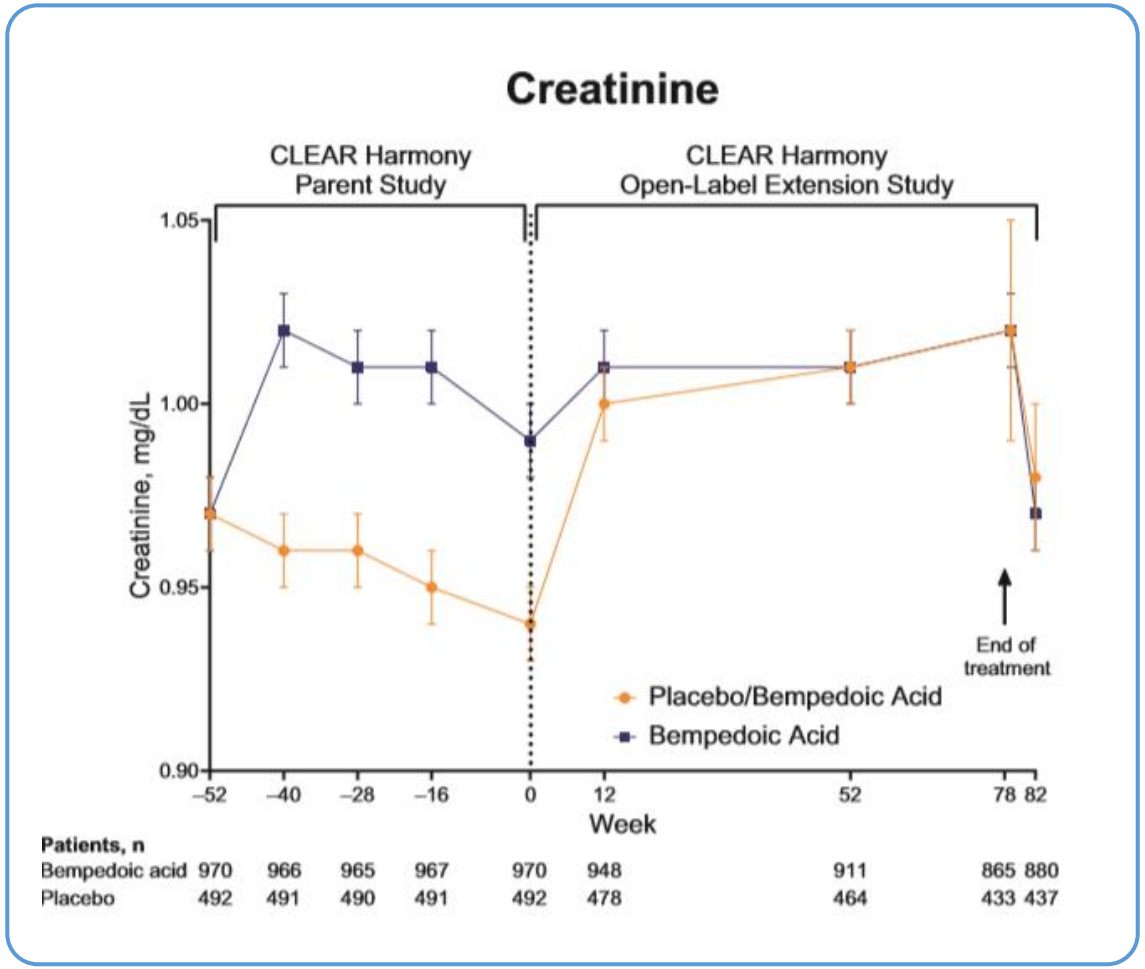
Ballantyne CM et al. Am J Cardiol 2022;174:1-11

Safety summary and most common drug-related treatment-emergent adverse events during the open-label extension study

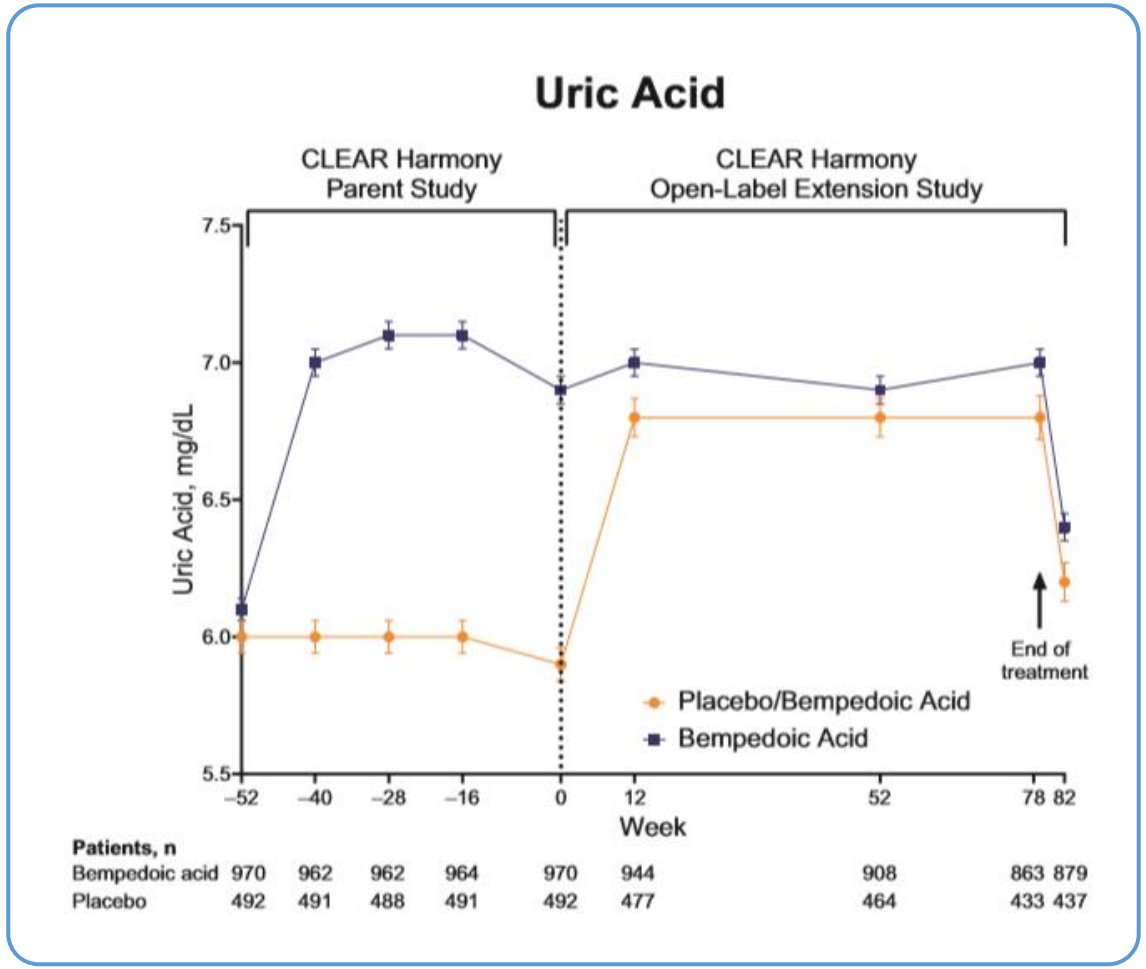
Parameter*	Patients, n (%)		
	Overall OLE study (n = 1,462)	Duration of bempedoic acid treatment	
		≤130 weeks (n = 970)	≤78 weeks (n = 492)
Safety overview			
Any TEAE	1143 (78.2%)	758 (78.1%)	385 (78.3%)
Serious TEAE	299 (20.5%)	202 (20.8%)	97 (19.7%)
TEAE leading to drug discontinuations	114 (7.8%)	69 (7.1%)	45 (9.1%)
TEAE with fatal outcome	13 (0.9%)	10 (1.0%)	3 (0.6%)
Most common drug-related TEAEs (≥0.5% in any group)			
Muscle spasms	25 (1.7%)	18 (1.9%)	7 (1.4%)
Myalgia	21 (1.4%)	14 (1.4%)	7 (1.4%)
Pain in extremity	10 (0.7%)	7 (0.7%)	3 (0.6%)
Arthralgia	9 (0.6%)	4 (0.4%)	5 (1.0%)
Dizziness	9 (0.6%)	7 (0.7%)	2 (0.4%)
Headache	8 (0.5%)	6 (0.6%)	2 (0.4%)
Aspartate aminotransferase increased	7 (0.5%)	3 (0.3%)	4 (0.8%)
Blood creatine phosphokinase increased	7 (0.5%)	6 (0.6%)	1 (0.2%)
Anemia	6 (0.4%)	3 (0.3%)	3 (0.6%)
Diarrhea	6 (0.4%)	3 (0.3%)	3 (0.6%)
Alanine aminotransferase increased	5 (0.3%)	2 (0.2%)	3 (0.6%)

Ballantyne CM et al. Am J Cardiol 2022;174:1-11

In patients treated with bempedoic acid, modest changes in creatinine and uric acid occur early, remain stable, and are reversible after treatment discontinuation



average increase: 0.05 mg/dL



average increase : 0,8 mg/dL

Ballantyne CM et al. Am J Cardiol 2022;174:1-11

Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients

the CLEAR Outcomes Investigators*

METHODS

We conducted a double-blind, randomized, placebo-controlled trial involving patients who were unable or unwilling to take statins owing to unacceptable adverse effects ("statin-intolerant" patients) and had, or were at high risk for, cardiovascular disease. The patients were assigned to receive oral bempedoic acid, 180 mg daily, or placebo. The primary end point was a four-component composite of major adverse cardiovascular events, defined as death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or coronary revascularization.

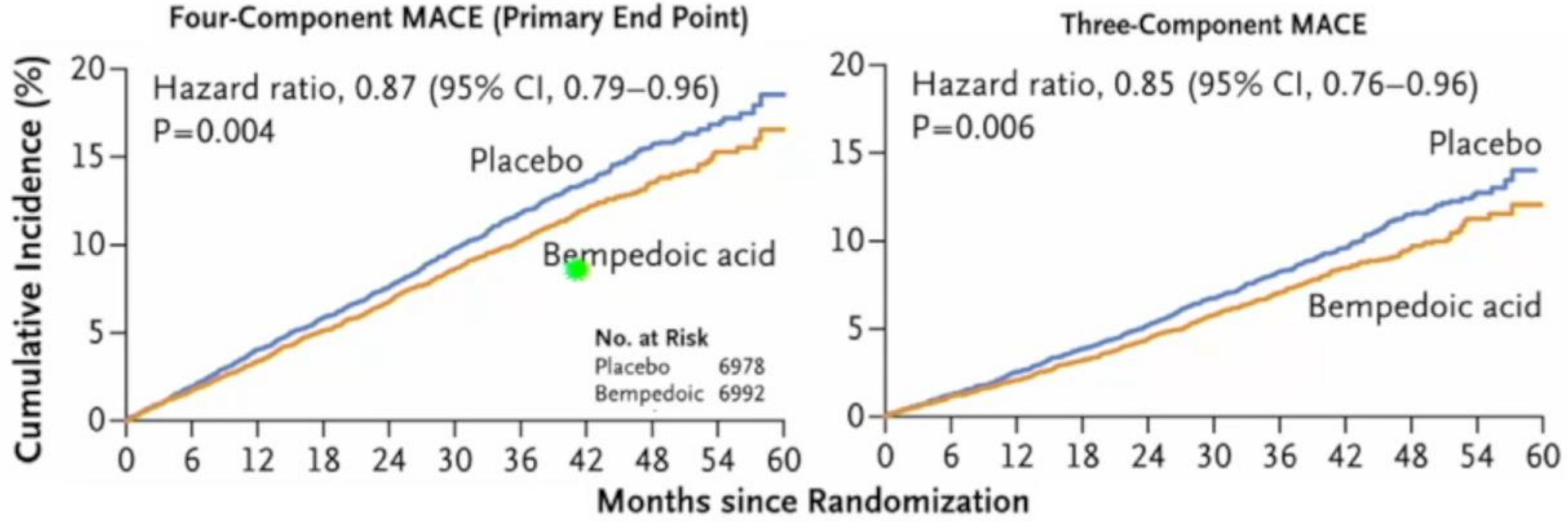
Nissen SE et al. N Engl J Med 388; April 13, 2023

CLEAR Outcomes: Selected Baseline Characteristics

Baseline characteristics	BA (N=6992)	Placebo (N=6978)
Age, years	65.5 ± 9.0	65.5 ± 8.9
Females, n (%)	3361 (48.1)	3379 (48.4)
Body mass index, kg/m^2	29.9 ± 5.2	30.0 ± 5.2
LDL-C mg/dL, mean (SD)	139.0 (34.9)	139.0 (35.2)
hsCRP mg/L, median (IQR)	2.3 (1.2 to 4.5)	2.3 (1.2 to 4.5)
Primary prevention, n (%)	2100 (30.0)	2106 (30.2)
Diabetes, n (%)	3144 (45.0)	3229 (46.3)
Baseline statin use, n (%)	1601 (22.9)	1573 (22.5)
Baseline EZE use, n (%)	803 (11.5)	809 (11.6)

Nissen SE et al. N Engl J Med 388; April 13, 2023

CLEAR Outcomes
Primary CV Endpoint



Nissen SE et al. N Engl J Med 388; April 13, 2023

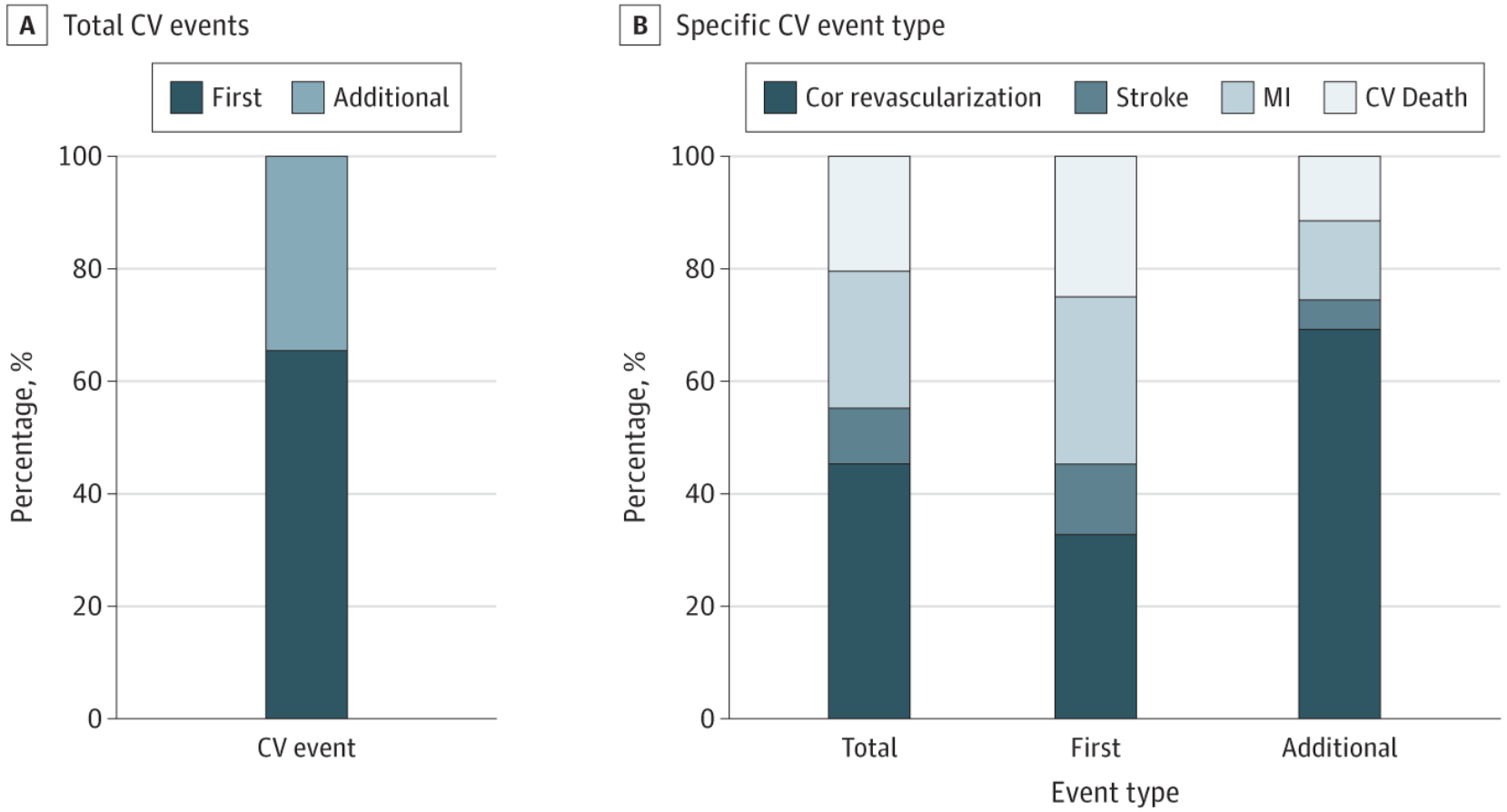
Adverse Events in 13.965 Patients in CLEAR Outcomes

	Bempedoic acid (N=7001)	Placebo (N=6964)
	Events (n), %	
Adverse events		
Any treatment emergent adverse event	6040 (86.3)	5919 (85.0)
Serious treatment emergent adverse event	1767 (25.2)	1733 (24.9)
Adverse event leading to drug discontinuation	759 (10.8)	722 (10.4)
Prespecified adverse events of special interest		
Myalgia **Discontinuation of treatment due to myalgia**	**393 (5.6)** **124 (1.8)**	**471 (6.8)** **129 (1.9)**
New onset diabetes in patients without diabetes at baseline	621/3856 (16.1)	640/3740 (17.1)
New onset diabetes in patients with pre-diabetes at baseline*	**569/2918 (19.5)**	**586/2877 (20.4)**
New onset diabetes in patients with normoglycaemia at baseline*	52/938 (5.5)	54/863 (6.3)
Worsening hyperglycaemia†	713/3145 (22.7)	746/3224 (23.1)
Hypoglycaemia	304 (4.3)	267 (3.8)

Nissen SE et al. N Engl J Med 388; April 13, 2023

Impact of Bempedoic Acid on Total Cardiovascular Events

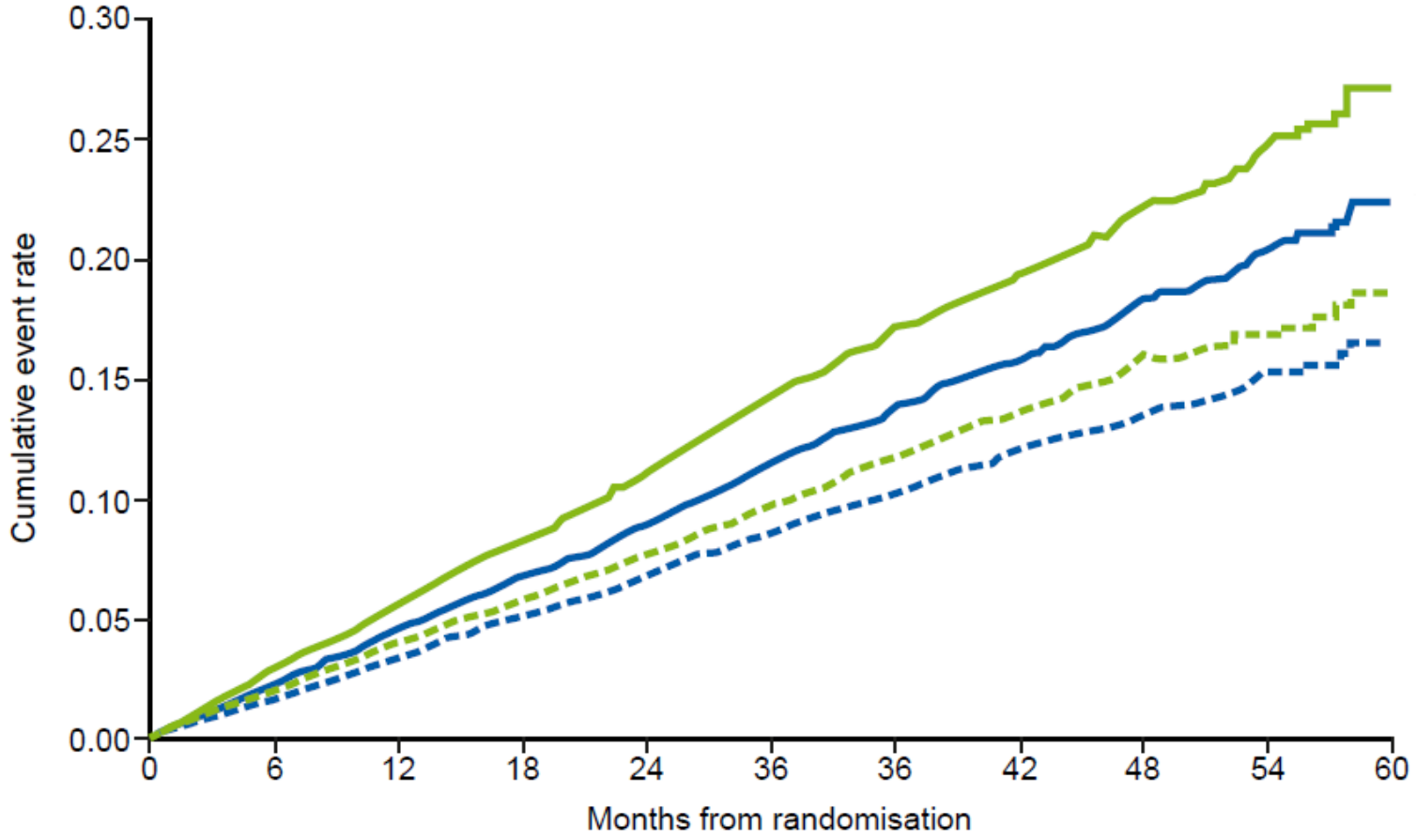
A Prespecified Analysis of the CLEAR Outcomes Randomized Clinical Trial



JAMA Cardiol January 17, 2024 2024;9:245-253

Impact of Bempedoic Acid on Total Cardiovascular Events

A Prespecified Analysis of the CLEAR Outcomes Randomized Clinical Trial



Total Events:
HR 0.80
(95% CI 0.72–0.89)

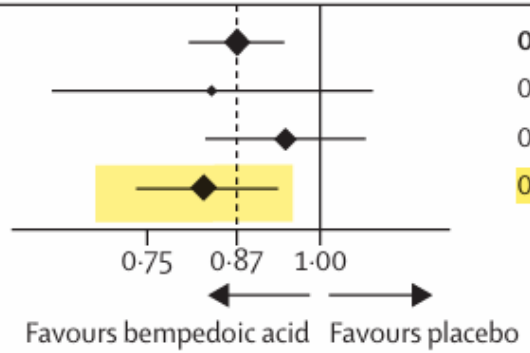
First Event:
HR 0.87
(95% CI 0.79–0.96)

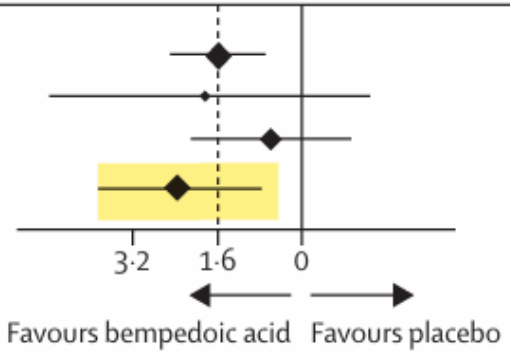
JAMA Cardiol January 17, 2024 2024;9:245-253

Efficacy and safety of bempedoic acid among patients with and without diabetes: prespecified analysis of the CLEAR Outcomes randomised trial

Relative and absolute risk reduction with bempedoic acid for MACE-4

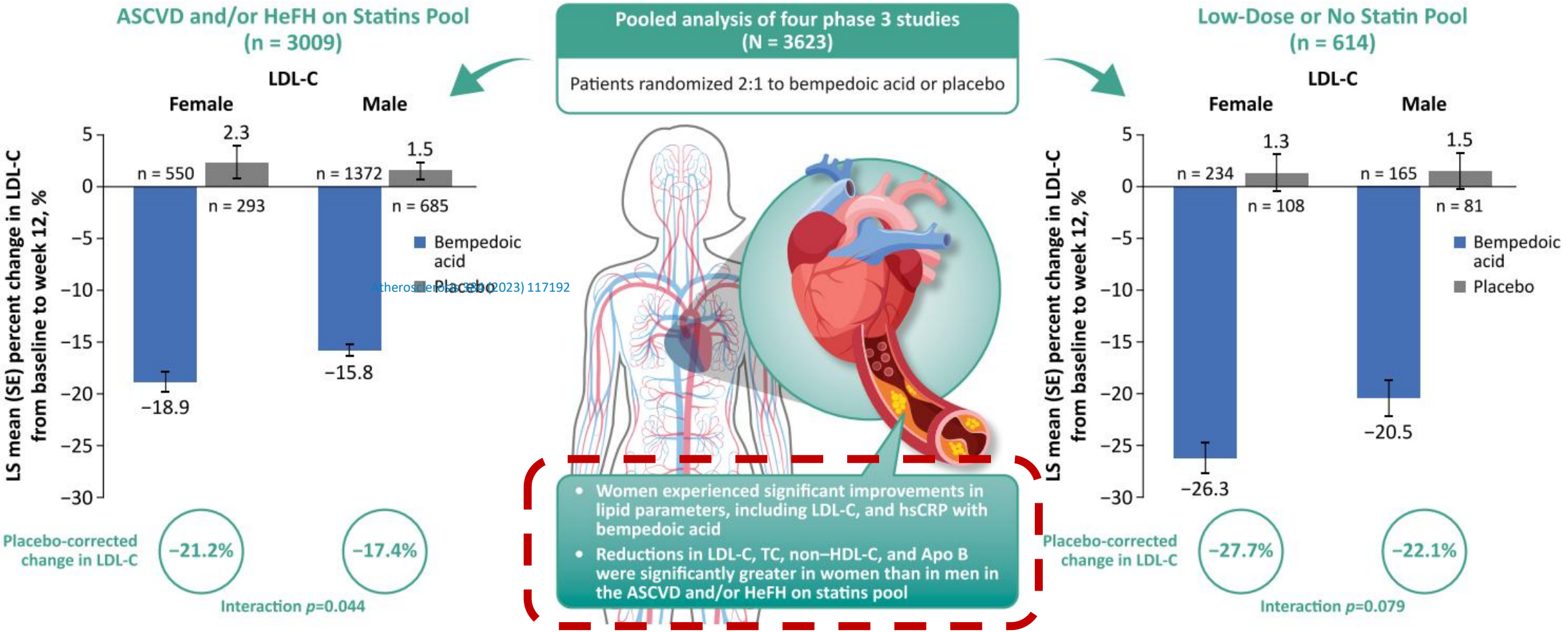
	Bempedoic acid n/N (%)	Placebo n/N (%)	HR Interaction p=0·42	HR (95% CI)	Absolute risk reduction (%) Interaction p=0·0063	Absolute reduction (95% CI)
Overall	819/6992 (11·7%)	927/6978 (13·3%)		0·87 (0·79 to 0·96)		1·6% (0·5 to 2·7%)
Normoglycemia	95/937 (10·1%)	103/864 (11·9%)		0·84 (0·63 to 1·10)		1·9% (–1·12 to 4·8%)
Prediabetes	350/2911 (12·0%)	364/2885 (12·6%)		0·94 (0·81 to 1·09)		0·6% (–1·1 to 2·3%)
Diabetes	374/3144 (11·9%)	460/3229 (14·2%)		0·83 (0·72 to 0·95)		2·4% (0·7 to 4·0%)





Ray KK et al. Lancet Diabetes Endocrinol 2024; 12: 19–28

Efficacy of bempedoic acid in women and men

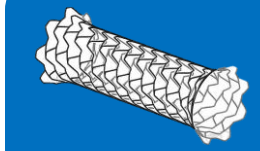


Atherosclerosis 2023, November

- ✓ **Was a new lipid-lowering therapy CLEARly necessary?**
- ✓ **Is it CLEAR how bembedoic acid works and how effective is?**
- ✓ **Is it CLEAR when and how to use bempedoic acid?**

I Profili Clinici per l'impiego di Acido Bempedoico

CLEAR PATH 2.0
il trattamento del paziente dislipidemico al CENTRO

- Paziente intollerante alla terapia con statine
-  Paziente sottoposto a PCI elettiva, senza storia di eventi avversi CV
- Paziente a rischio cardiovascolare Moderato, Alto e Molto Alto, senza storia di eventi CV
- Paziente con Sindrome Coronarica Cronica
-  Paziente Diabetico
- Paziente con storia di Ictus Ischemico non cardioembolico e/o Arteriopatia Carotidea
-  Paziente Anziano
-  Paziente con Arteriopatia Periferica

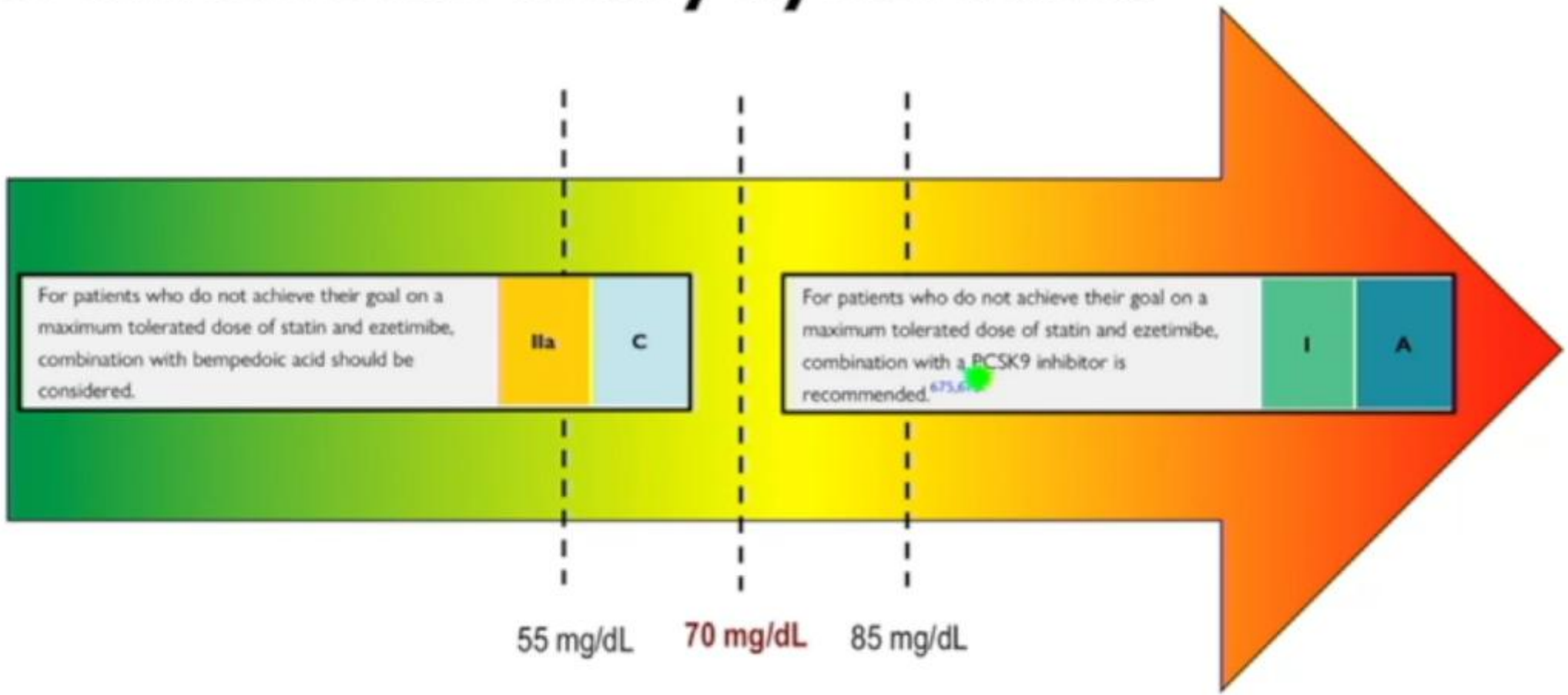
2025 ESC/EAS Guidelines Recommendations for Pharmacological LDL-C Lowering

Recommendations	Class[a]	Level[b]
Non-statin therapies with proven cardiovascular benefit,[c] taken **alone or in combination**, **are recommended for patients who are unable to take statin therapy** to lower LDL-C levels and reduce the risk of CV events. The choice should be based on the magnitude of additional LDL-C lowering needed.	I	A
Bempedoic acid is recommended in patients who are unable to take statin therapy to achieve the LDL-C goal.	I	B
The **addition of bempedoic acid to the maximally tolerated dose of statin with or without ezetimibe** should be considered in **patients at high or very high risk** in order to achieve the LDL-C goal.	IIa	C

Mach F, et al. Eur Heart J 2025;00:1–20

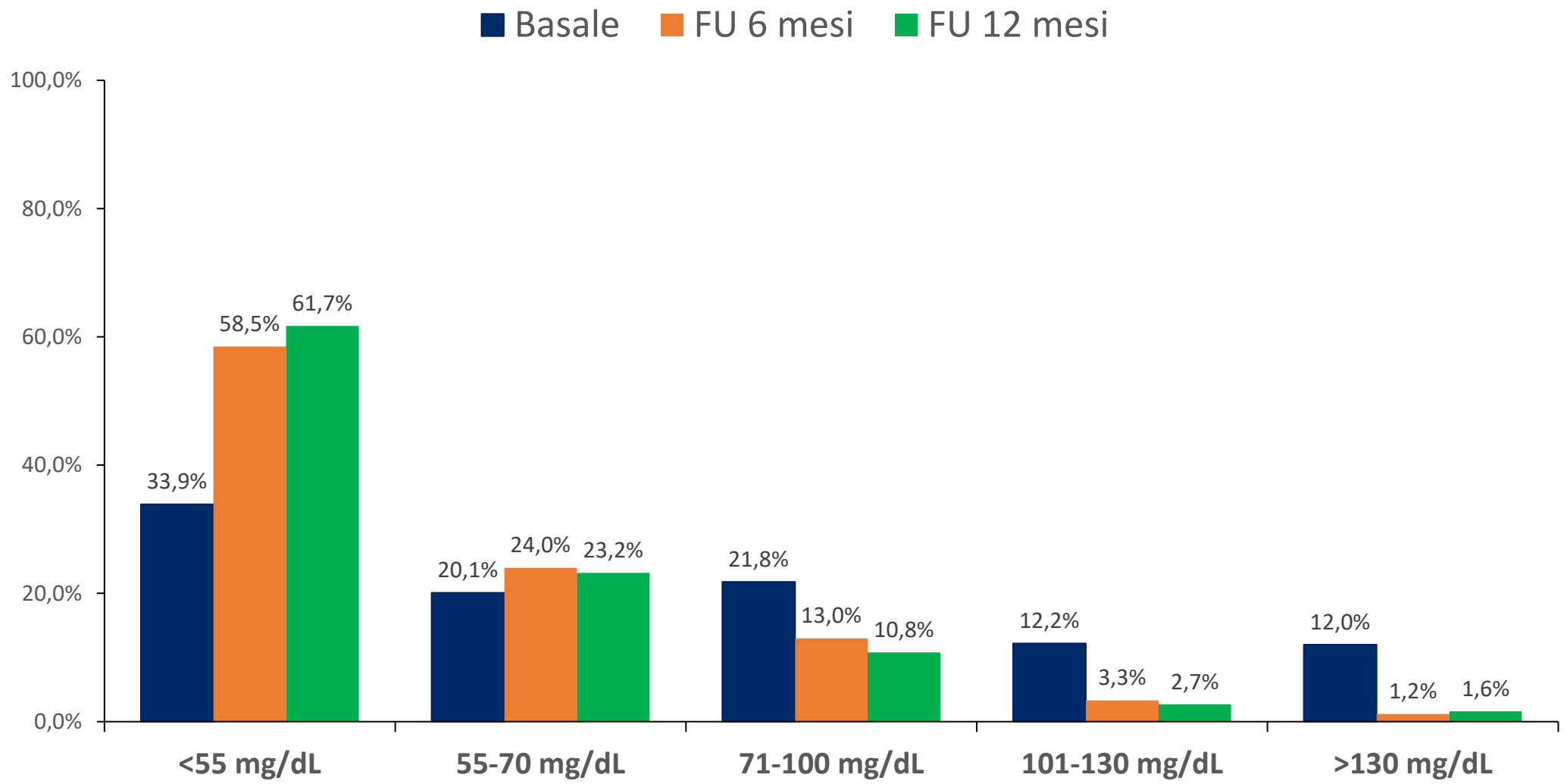
European Heart Journal (2024) **45**, 3415–3537

2024 ESC Guidelines for the management of chronic coronary syndromes



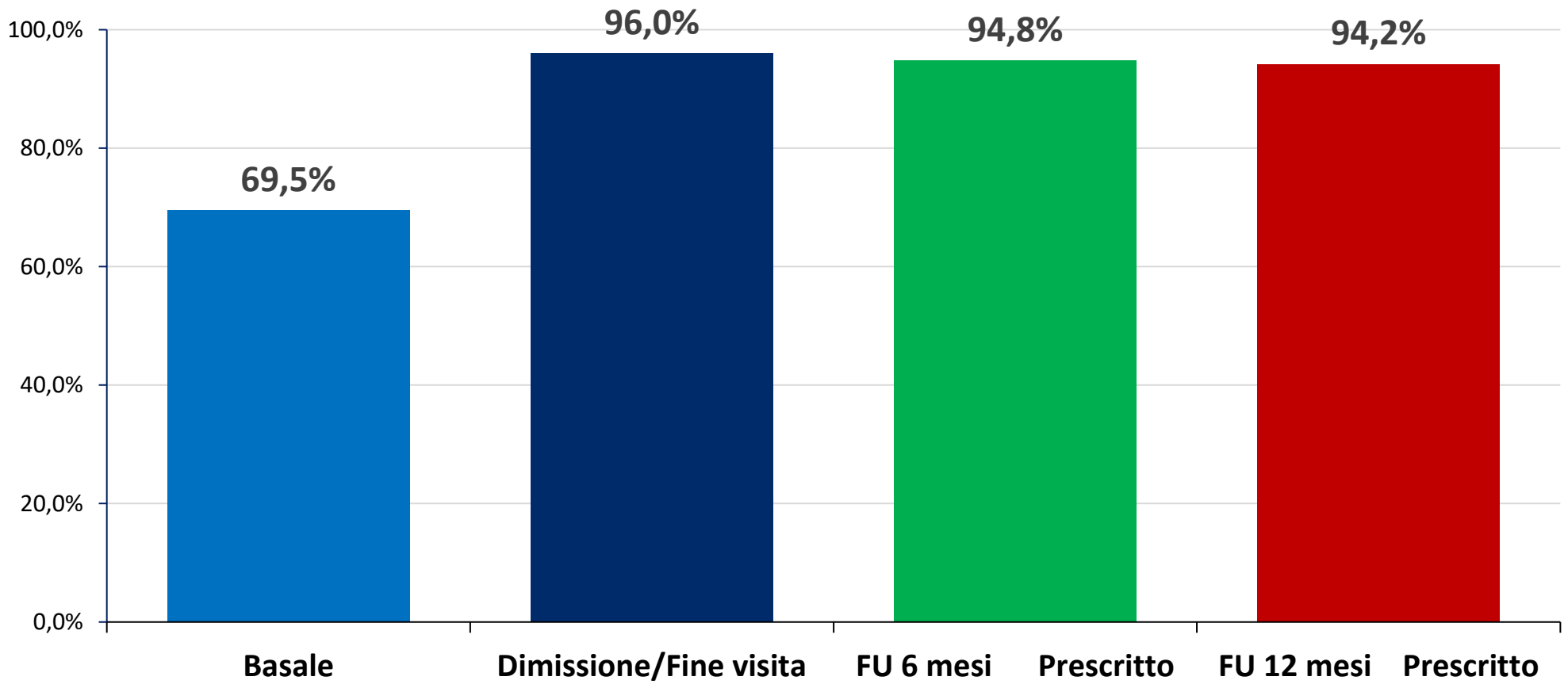
BRING•UP PREVENZIONE

Colesterolo LDL (3737 pts)



BRING•UP PREVENZIONE

Utilizzo di statine (n. 4180)



BRING•UP PREVENZIONE

Altri ipolipemizzanti prescritti (n. 4180)

Farmaco	Basale n. (%)	FU a 6 mesi Post-visita n. (%)	FU a 12 mesi Post-visita n. (%)
Almeno un altro ipolipemizzante	3329 (79.6)	3624 (86.7)	3688 (88.2)
Ezetimibe	3243 (77.6)	3527 (84.4)	3560 (85.2)
Fibrati	32 (0.8)	32 (0.8)	35 (0.8)
Evolocumab	133 (3.2)	152 (3.6)	168 (4.0)
Alirocumab	149 (3.6)	178 (4.3)	211 (5.1)
Inclisiran	63 (1.5)	95 (2.3)	106 (2.5)
Acido Bempedoico	**188 (4.5)**	**376 (9.0)**	**444 (10.6)**

La terapia di associazione con acido bempedoico: quali prospettive