

The Next Step in Getting Patients To Goal

March 6, 2023



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Agenda

-  Opening Remarks
-  CLEAR Outcomes Data
-  Importance of CVOT and Bempedoic Acid
-  Commercial Update
-  FY 2023 Financial Guidance

Speaker Profiles



Sheldon Koenig
President & CEO, Esperion



JoAnne Foody, MD, FACC, FAHA
Chief Medical Officer, Esperion



Steven E. Nissen, MD
Principal Investigator for CLEAR Outcomes



Eric Warren, R.Ph.
Chief Commercial Officer, Esperion



BJ Swartz
Chief Strategy Officer, Esperion



Ben Halladay
Chief Financial Officer, Esperion

CLEAR Outcomes – A Game Changer for Esperion

1

We have a unique and successful outcome study in a large therapeutic category that demonstrates the benefits of bempedoic acid, the active ingredient in NEXLETOL® & NEXLIZET®

2

We are poised for a major inflection in sales and prescriptions and are targeting blockbuster status

3

Based on the robustness of the CLEAR Outcomes data, we believe we would be entitled to receive \$300 million in milestone payments from collaborative partners upon inclusion of cardiovascular risk reduction data in the European label and up to \$140 million upon other regulatory milestones

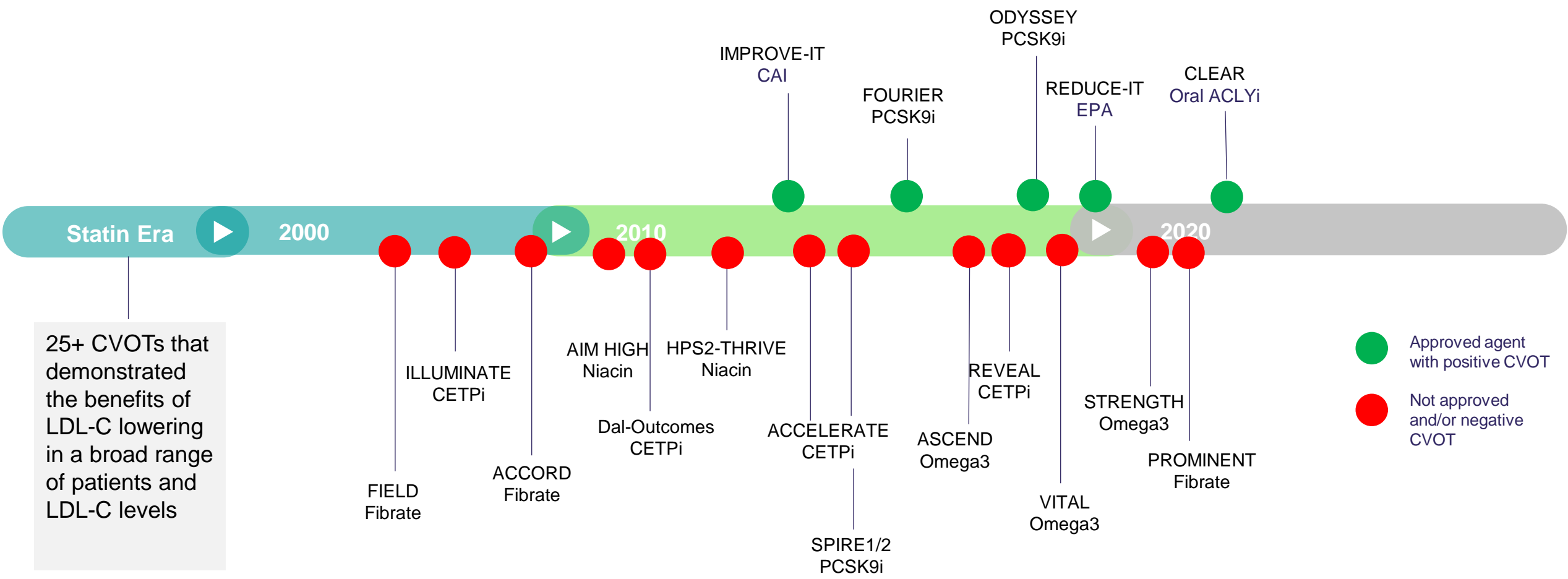


What's Next? Importance of CVOT and Bempedoic Acid

JoAnne Foody, MD, FACC, FAHA

Chief Medical Officer

First Non-Statin Lipid Lowering Therapy with Positive CVOT



25+ CVOTs that demonstrated the benefits of LDL-C lowering in a broad range of patients and LDL-C levels

● Approved agent with positive CVOT
● Not approved and/or negative CVOT

*In patients with controlled LDL-C but elevated TGs



A Real Game Changer - Landmark CLEAR Outcomes Study

First-of-its-kind, unprecedented CVOT in patients unable to maximize or tolerate a statin

Focused on significant, underserved population unable to maximize or tolerate statins



Over 14,000 patients in 32 countries



~50% women



Primary Endpoint (MACE-4): Composite of the time to first cardiovascular death, nonfatal myocardial infarction, non-fatal stroke, or coronary revascularization

Hierarchy of Secondary Endpoints:

- MACE-3
- Fatal and non-fatal MI
- Coronary revascularization
- Fatal and non-fatal stroke
- Death from cardiovascular causes
- All-cause mortality

THE CLEAR Program >60,000 Patients in >30 Countries

Large integrated, scientifically rigorous program to establish bempedoic acid as a new standard of care

Lipid Lowering		Outcomes	Healthcare System Partnerships	Implementation Science & Real-World Evidence
Registration Trials – Phase 3		Primary/Secondary Prevention	US Healthcare Systems	Initiation of Treatment
CLEAR Serenity	1002-050	CLEAR Outcomes	UT Southwestern Medical Center Baylor Scott & White/VA* Durham VA Medical Center*	FCQN-Spencer Health Program PAD Alert
CLEAR Harmony	1002FDC-053			
CLEAR Tranquility				
CLEAR Wisdom				
Registration Trials – Phase 2			NHS	Post-ACS
1002-008	1002-006		UK NHS Clinical audit	CLEAR ACS
1002-038	1002-009			
1002-039	1002-035			
1002-003	1002-007			
1002-005	1002-014			
Diverse Patient Populations				
CLEAR Path 1 (pediatrics)				
Lactation study*				
Pregnancy study				
End Stage Renal Disease*				

*Planned



Data Drives Meaningful Label Expansion Potential

Many more patients can potentially benefit

Before

INDICATION:

- Adjunct to diet and maximally tolerated statin therapy
- For the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C

LIMITATIONS:

- Cardiovascular morbidity and mortality effect has not been determined

**Positive
CVOT**

After

POTENTIAL LABEL IMPLICATIONS:

- Additional indication: REDUCE THE RISK OF CARDIOVASCULAR EVENTS in patients with established CVD or at high risk for CVD
- Post CVOT Potential Label Modifications:
 - Removes maximally tolerated statin therapy
 - Expands to primary and secondary prevention

NEXLETOL[®] & NEXLIZET[®] - Optimized to Address Unmet Medical Need

Based on robust data, NEXLETOL/NEXLIZET designed for use alone or in combination with statins to improve outcomes.

- Statins remain first-line therapy to reduce the risk of major adverse cardiovascular events.^{1,2}
- Lower dose statin and withdrawal from statin therapy is associated with increased risk of adverse cardiovascular events.^{3,4}
- Up to 30% of patients are unable to tolerate guideline-recommended doses of statins.^{5,6}
- Bempedoic Acid (contained in both NEXLETOL and NEXLIZET) is specifically designed as a prodrug activated in only in the liver to specifically reduce the likelihood of statin-associated adverse effects and fewer drug-drug interactions.^{7,8}
- The **CLEAR Program** has assessed the impact of NEXLETOL/NEXLIZET in combination with statin or alone on key endpoints including LDL lowering and CV outcomes



New England Journal of Medicine Editorials

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL



SCIENCE BEHIND THE STUDY

Bempedoic Acid and the Prevention of Cardiovascular Disease

John F. Keane, Jr., M.D.

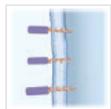
In an article now published in the *Journal*, Nissen and colleagues report the results of the CLEAR (Cholesterol Lowering via Bempedoic Acid, an ACL-Inhibiting Regimen) Outcomes trial, which tested the effect of bempedoic acid in patients with or at increased risk for cardiovascular disease.¹ Patients who were unable or unwilling to take high-intensity statins because of unacceptable adverse effects (“statin-intolerant” patients) were the target trial population; statins are typically used as first-line agents to prevent cardiovascular events in patients at high cardiovascular risk. Nissen et al. found that the percent reduction in the LDL cholesterol level was 21 percentage points greater with bempedoic acid than with placebo. This reduction in cholesterol level corresponded to a 13% lower risk of major adverse cardiovascular events, defined as a four-component composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or coronary revascularization. These results are discussed in an accompanying editorial² and are welcome news for a patient population in which it is otherwise very challenging to achieve

Key Concepts



Prodrug

A therapeutic agent that is delivered in an inactive form and is metabolized to its active form in vivo.



Protein prenylation

The addition of farnesyl or geranylgeranyl moieties (both of which are hydrophobic) to proteins, which facilitates their attachment to membranes.

 An expanded illustrated glossary is available at [NEJM.org](https://www.nejm.org)

response, cholesterol-depleted cells up-regulate low-density lipoprotein (LDL) receptors on the cell surface to internalize more cholesterol for cellular needs (Fig. 1). In the liver, this process affords increased removal of cholesterol-rich LDL particles from the circulation, which explains the LDL cholesterol-lowering effect of statins

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL



Benefits of Bempedoic Acid — Clearer Now

John H. Alexander, M.D., M.H.S.

Vascular atherosclerosis begins in young adulthood and progresses over decades. The condition is associated with considerable morbidity and mortality from coronary, cerebrovascular, and peripheral vascular disease. The foundation of contemporary prevention and treatment of atherosclerosis is lowering the serum cholesterol level with 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (statins). Statins reduce the low-density lipoprotein (LDL) cholesterol level, slow the progression of atherosclerosis, and reduce the morbidity and mortality associated with coronary, cerebrovascular, and peripheral vascular events.¹ High-intensity statin therapy is recommended for all patients with established atherosclerotic vascular disease, as well as those at high risk for atherosclerotic vascular disease.² Unfortunately, a sizable percentage (approximately 10%) of those who would

ial hypercholesterolemia.⁸⁻¹⁰ Bempedoic acid is a prodrug that is metabolized to its active metabolite in the liver but not in peripheral tissues and thus has few, if any, muscle-related side effects.⁹ What has been lacking to date is high-quality evidence that bempedoic acid reduces the risk of clinical events.

In an article now published in the *Journal*, Nissen et al. begin to fill this gap with the results of the CLEAR (Cholesterol Lowering via Bempedoic Acid [ECT1002], an ACL-Inhibiting Regimen) Outcomes trial.¹¹ A total of 13,970 patients who had or were at high risk for atherosclerotic vascular disease and were unable to take more than a very low dose of a statin were randomly assigned to receive bempedoic acid (180 mg daily) or placebo. The percent reduction in the LDL cholesterol level was greater with bempedoic acid than with placebo by 21 percent-



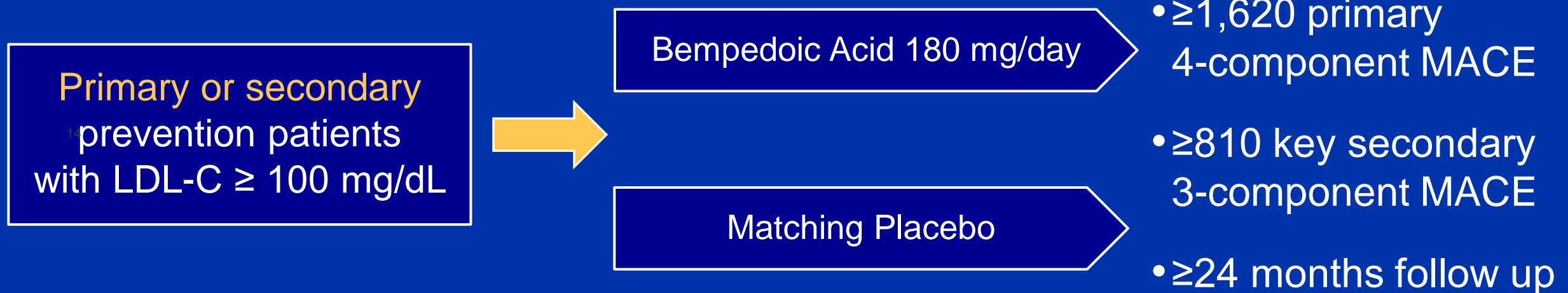
CLEAR Outcomes Data

Steven E. Nissen, MD

Principal Investor for CLEAR Outcomes

CLEAR Outcomes Trial Design

- Statin intolerance: An adverse effect that started or increased during statin therapy and resolved or improved after therapy discontinued.
- Intolerance to 2 or more statins or 1 statin if unwilling to attempt a second statin or advised by physician to not attempt second statin. Very low dose statin therapy permitted (< lowest approved dose).



Primary and Key Secondary Endpoints

- Primary endpoint 4-component MACE: nonfatal MI, nonfatal stroke, coronary revascularization or cardiovascular death
- Hierarchical testing of key secondary endpoints:
 - 1) 3-component MACE (MI, stroke or CV death)
 - 2) Fatal and nonfatal MI
 - 3) Coronary revascularization
 - 4) Fatal and nonfatal stroke
 - 5) Cardiovascular death
 - 6) All-cause mortality



Sequential
Testing

Study Milestones

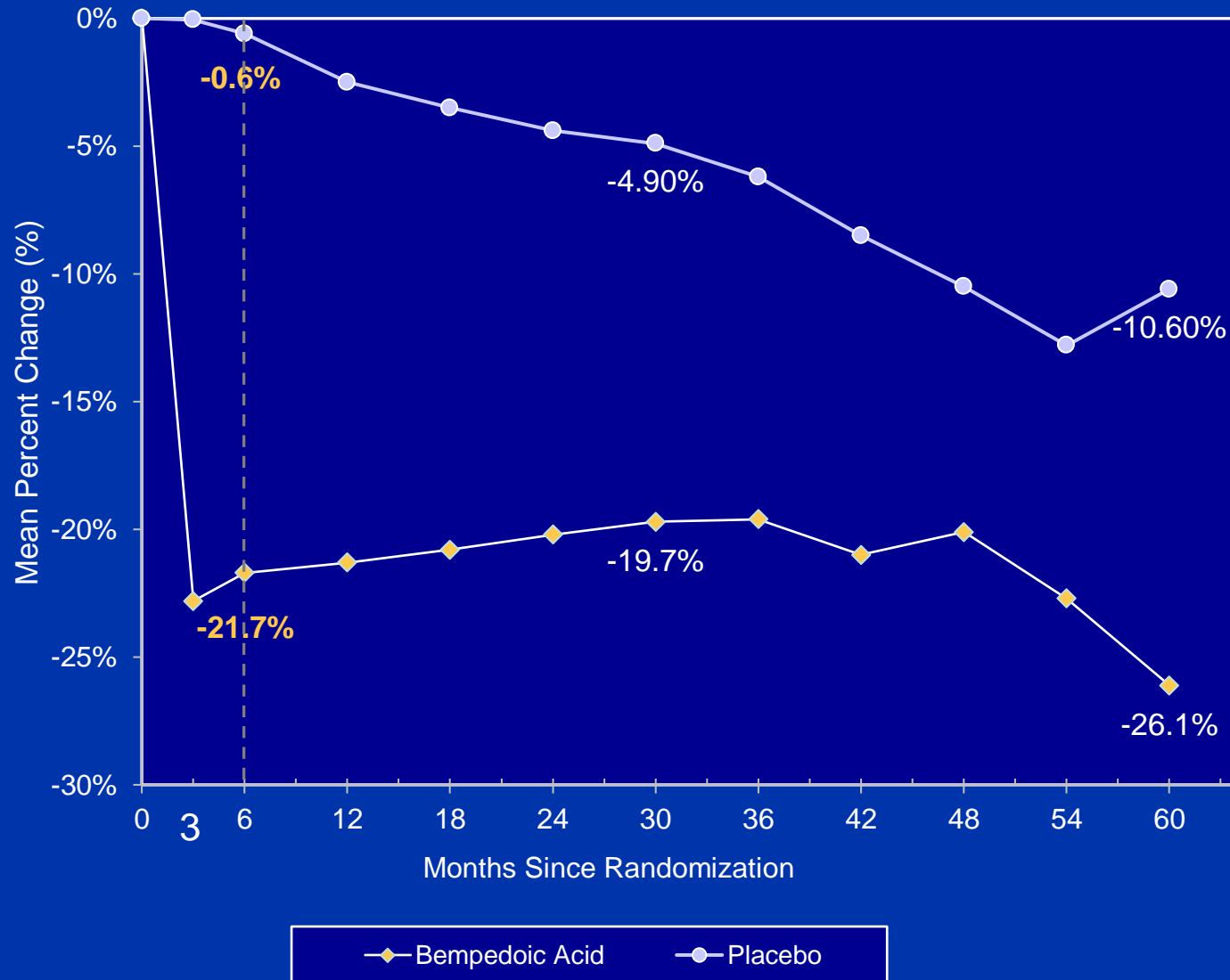
- 13,970 patients randomized at 1250 sites in 32 countries.
- Patients enrolled December 2016 to August 2019 with median duration of follow-up 40.6 months.
- Despite the pandemic, complete assessment for the primary endpoint in 95.3% and vital status in 99.4% of patients.
- 4-component MACE occurred in 1746 patients and 3-component MACE in 1238 patients.

Selected Baseline Characteristics

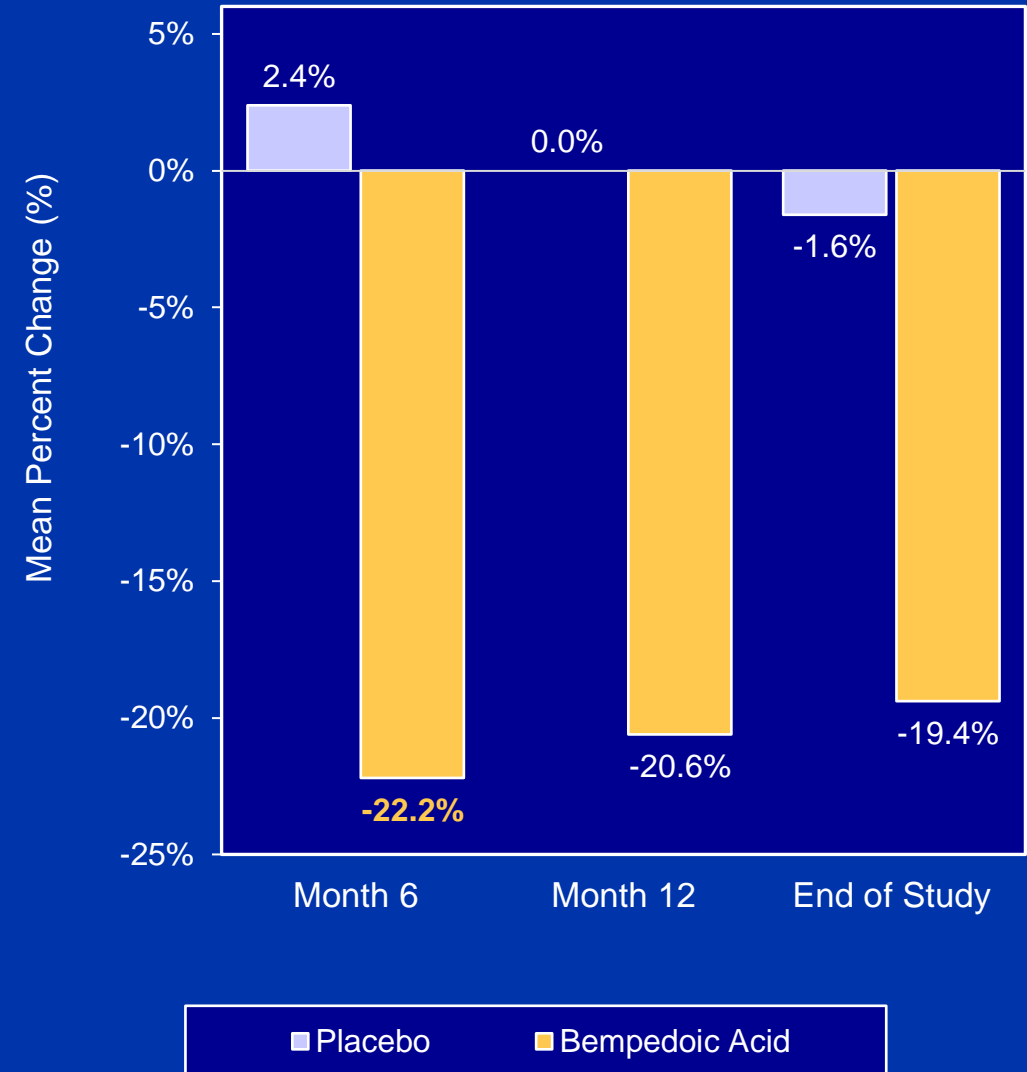
Characteristic	Bempedoic Acid N=6992	Placebo N=6978
Mean Age (years)	65.5	65.5
Female sex	48.1%	48.4%
White	91.5%	90.8%
LDL cholesterol (mg/dL)	139.0	139.0
HDL cholesterol (mg/dL)	49.6	49.4
hsCRP (mg/L)	2.3	2.3
High Risk Primary Prevention	30.0%	30.2%
Secondary Prevention	70.0%	69.8%
Diabetes	45.0%	46.3%
Baseline statin use	22.9%	22.5%

Effect of Trial Regimens on LDL-C and hsCRP

Percent Change in LDL-C over Time

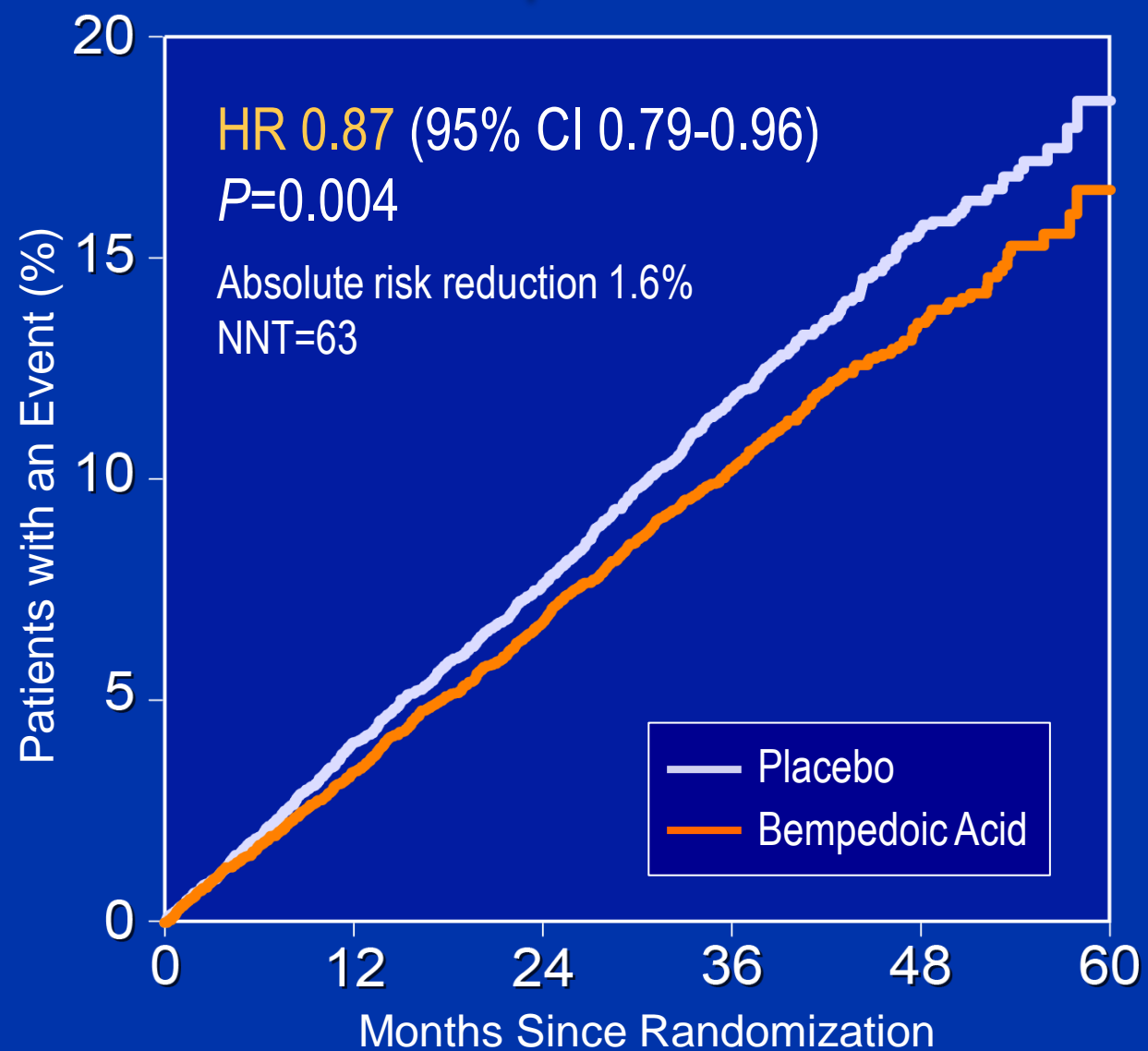


Percent Change in hsCRP

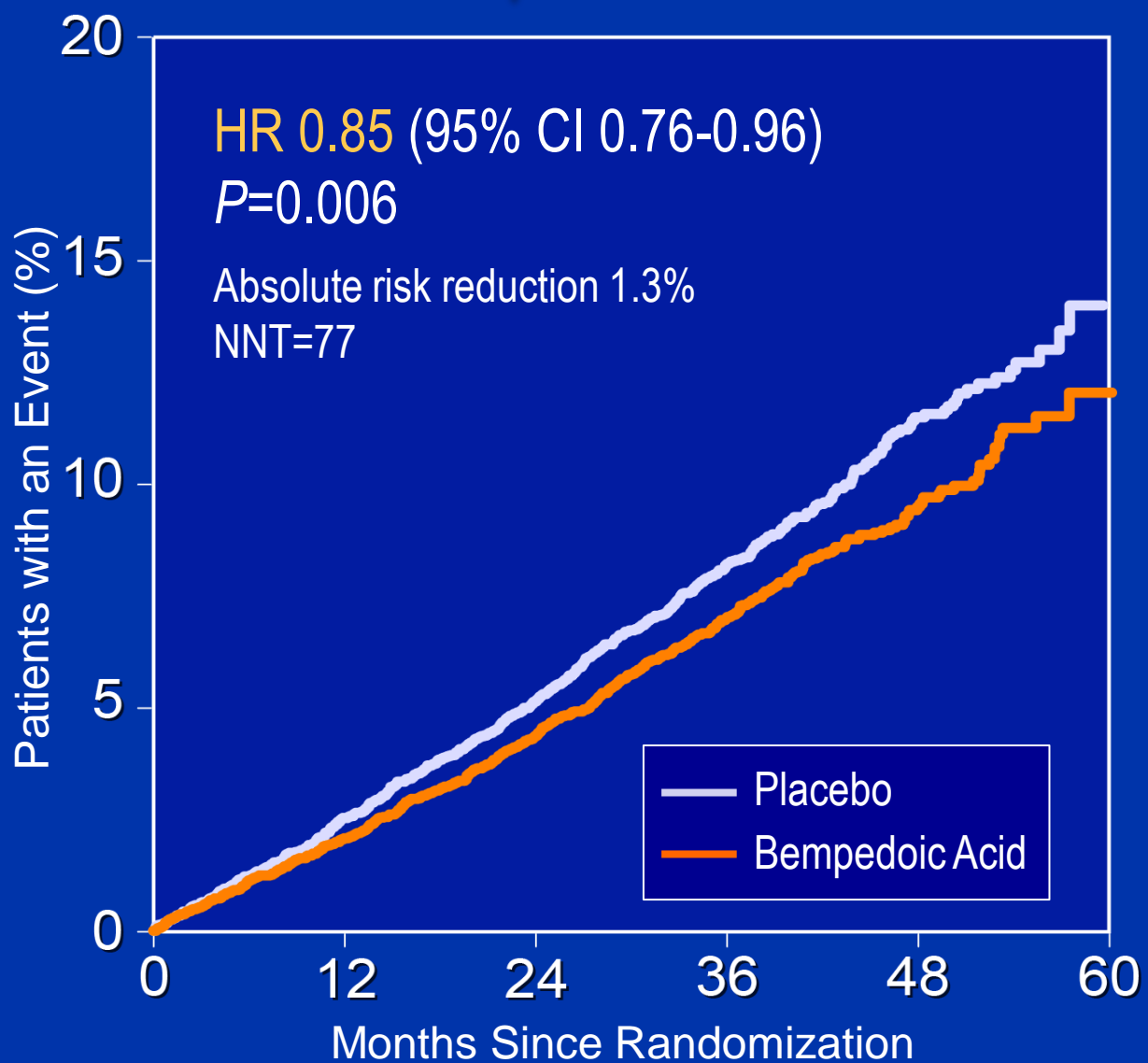


Primary and First Key Secondary Cardiovascular End Points

4-component MACE

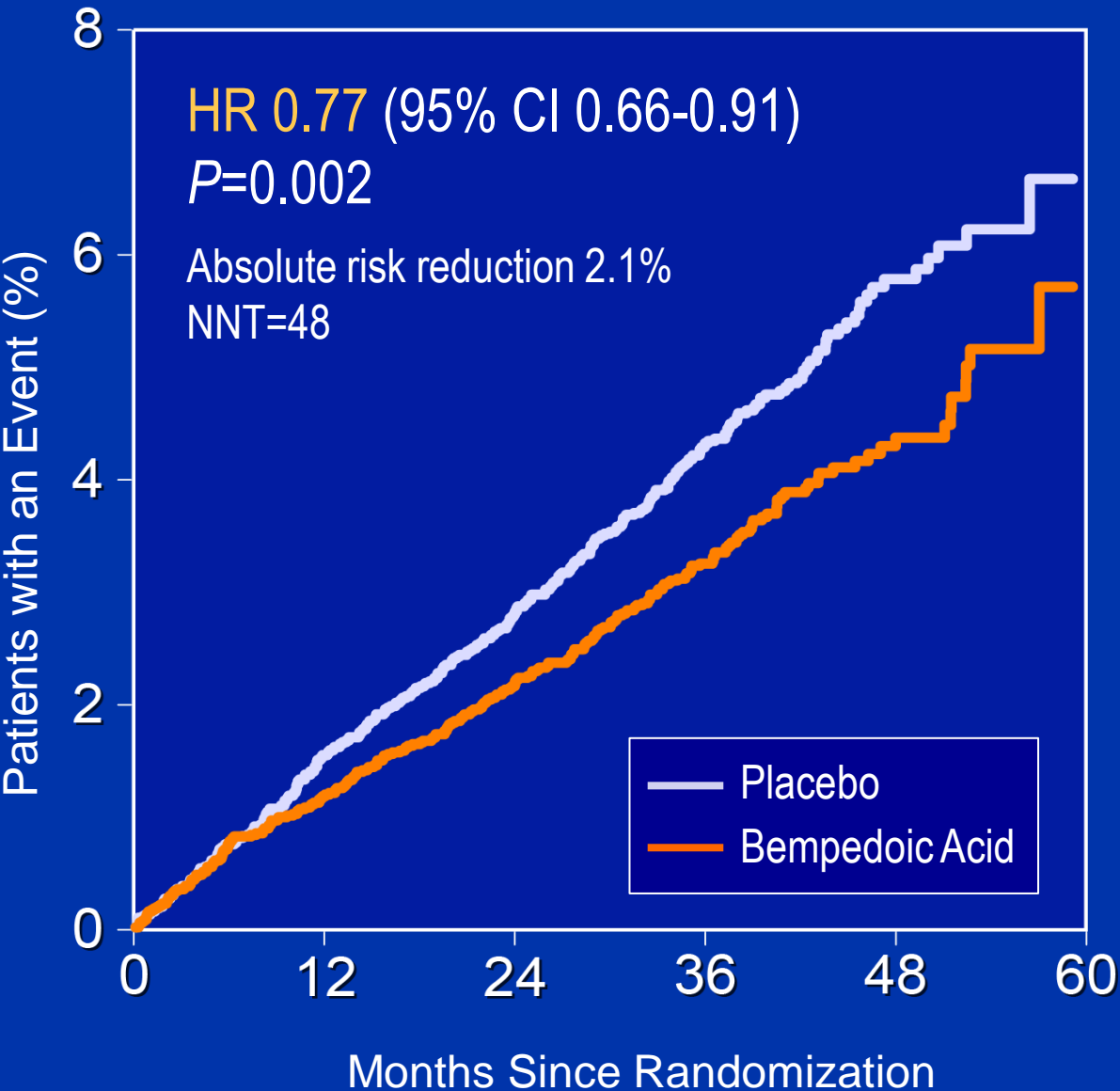


3-component MACE

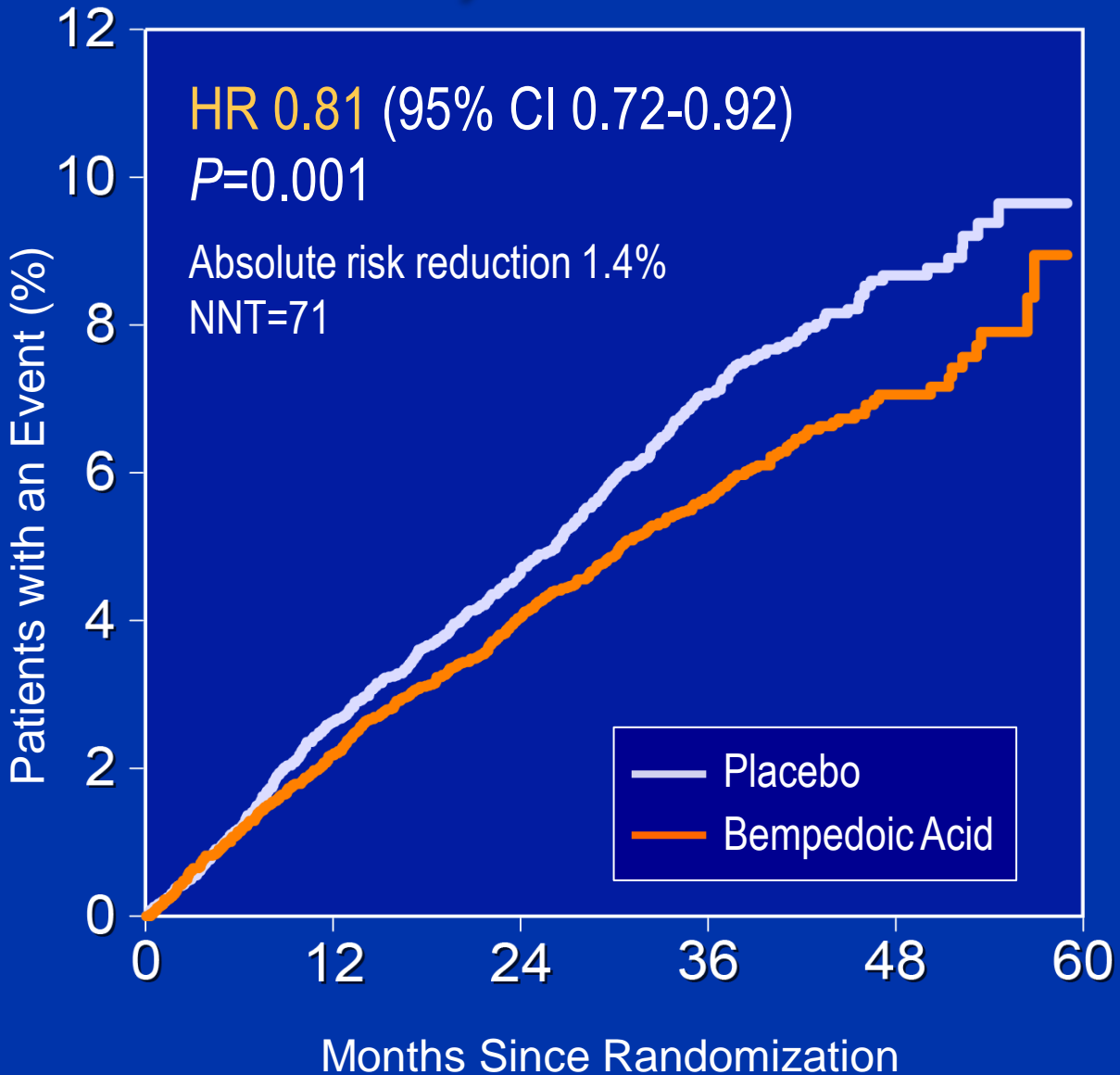


Key Secondary End Point: MI and Coronary Revascularization

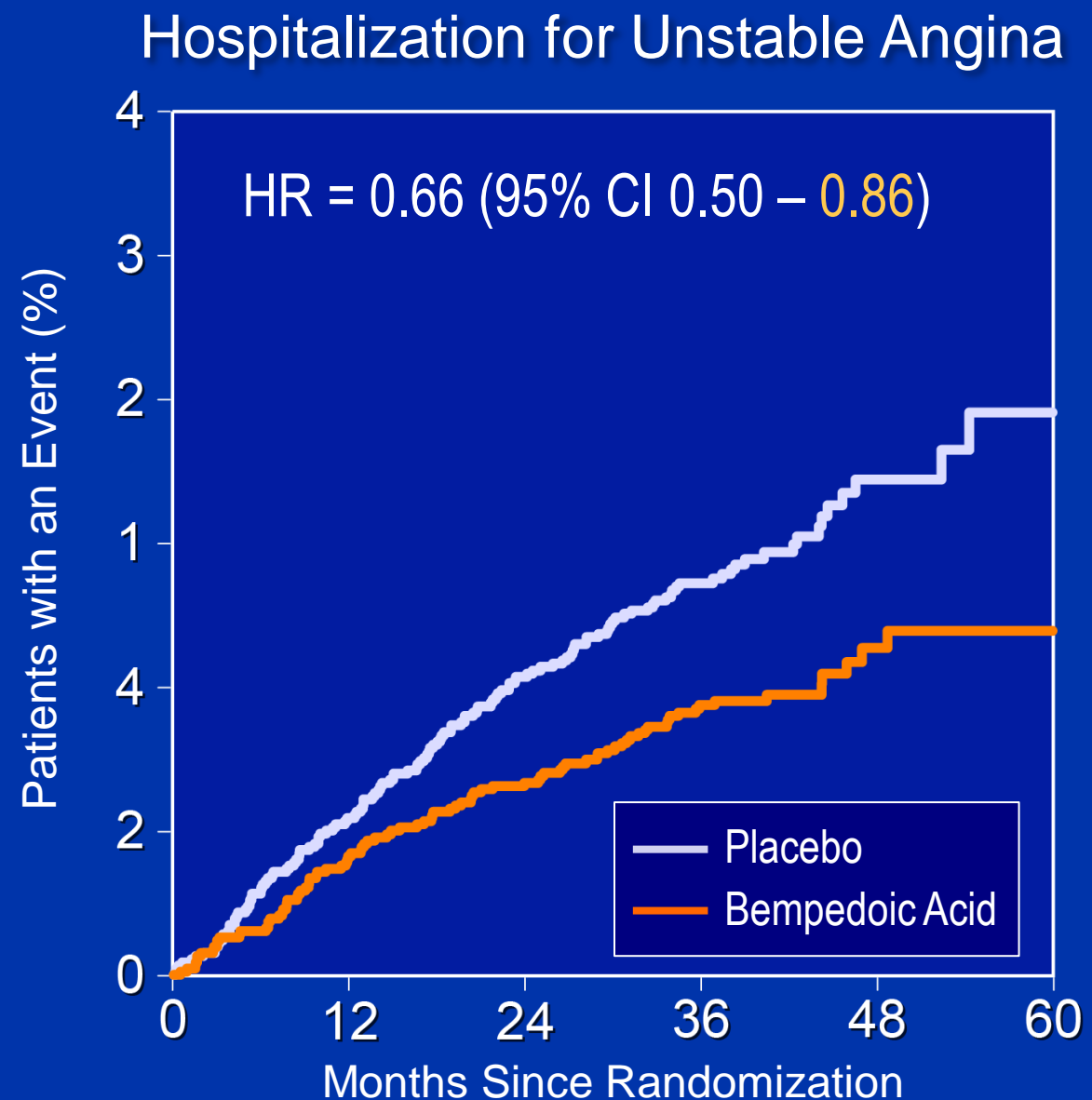
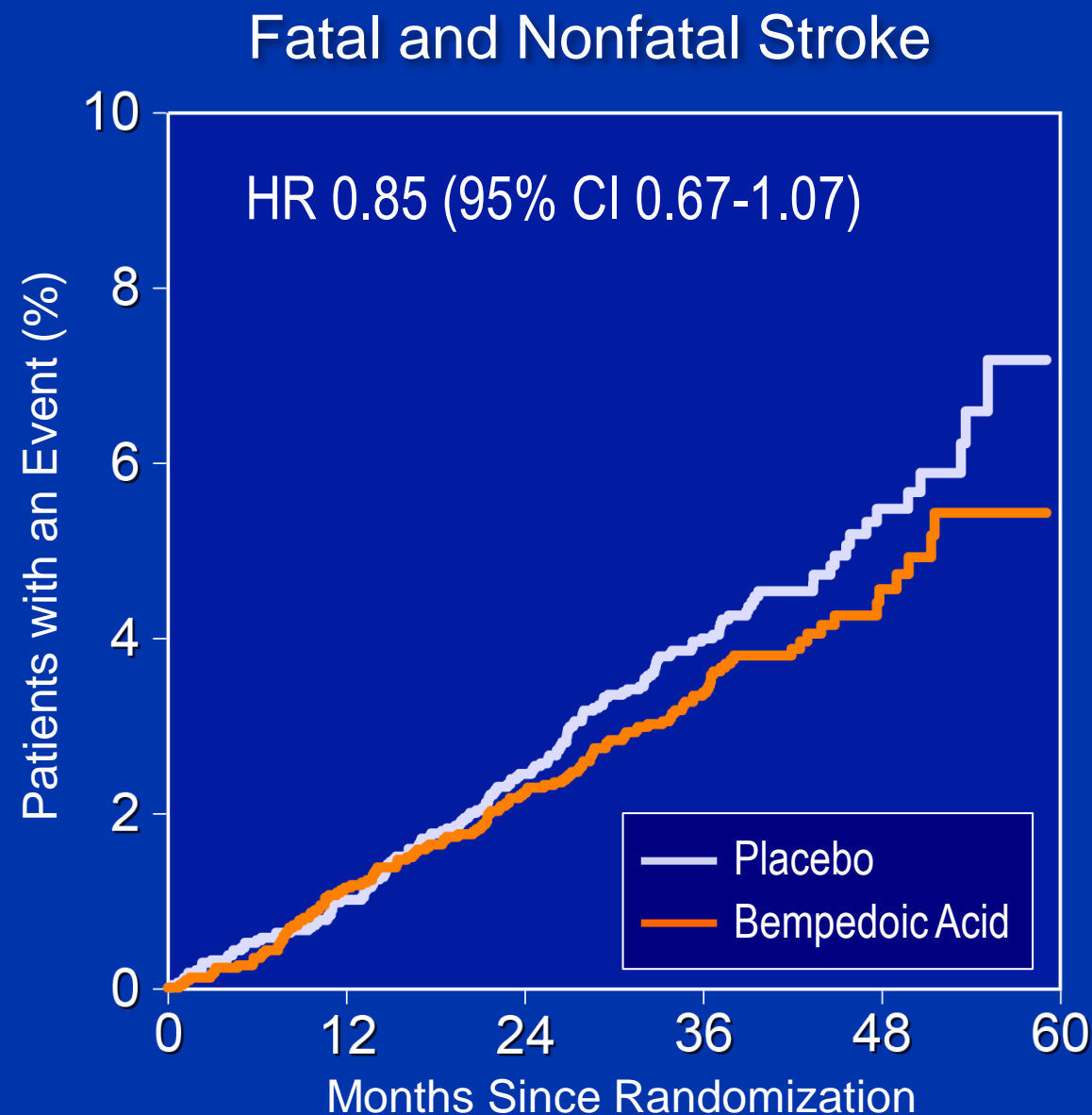
Fatal and Nonfatal MI



Coronary Revascularization

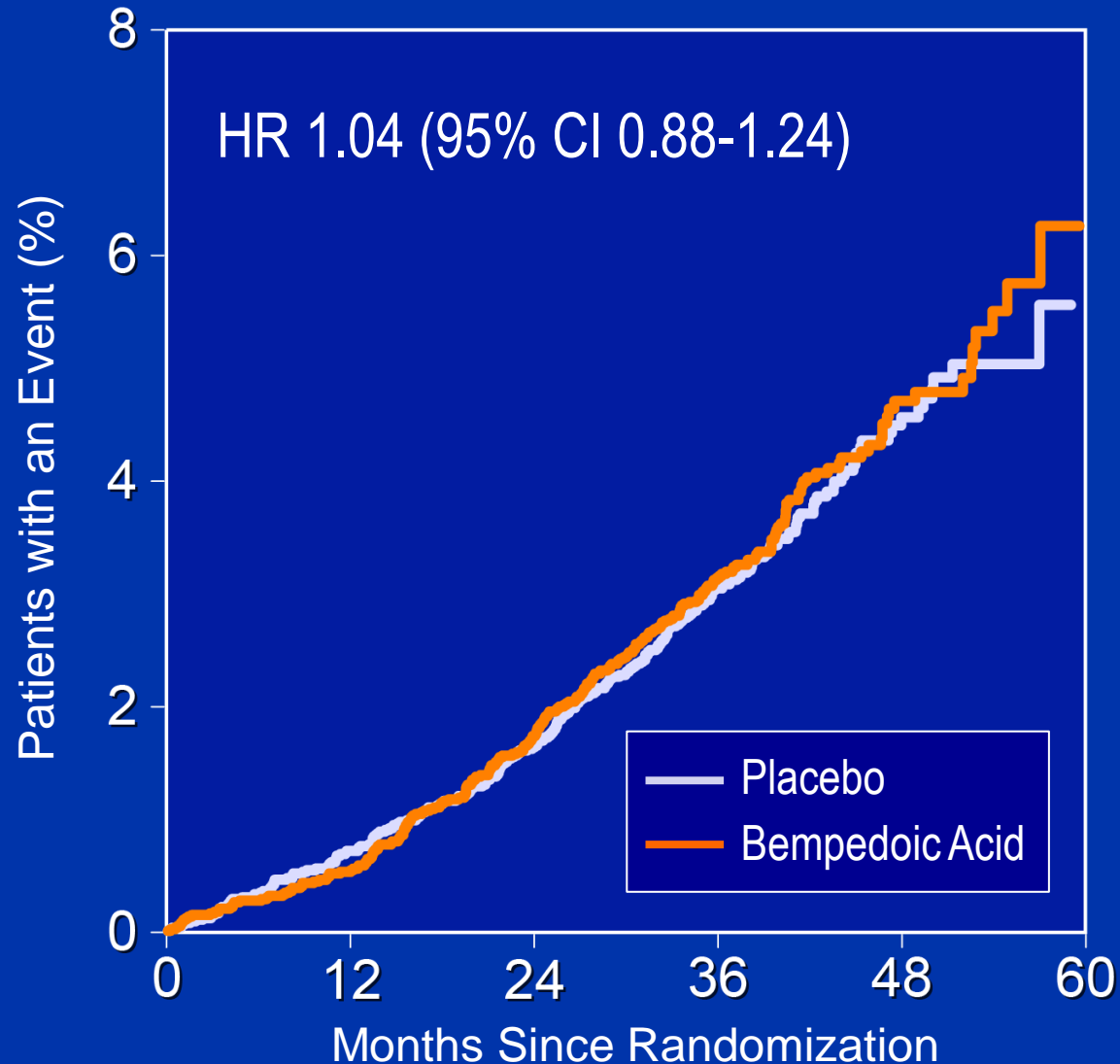


Effect on Stroke and Hospitalization for Unstable Angina

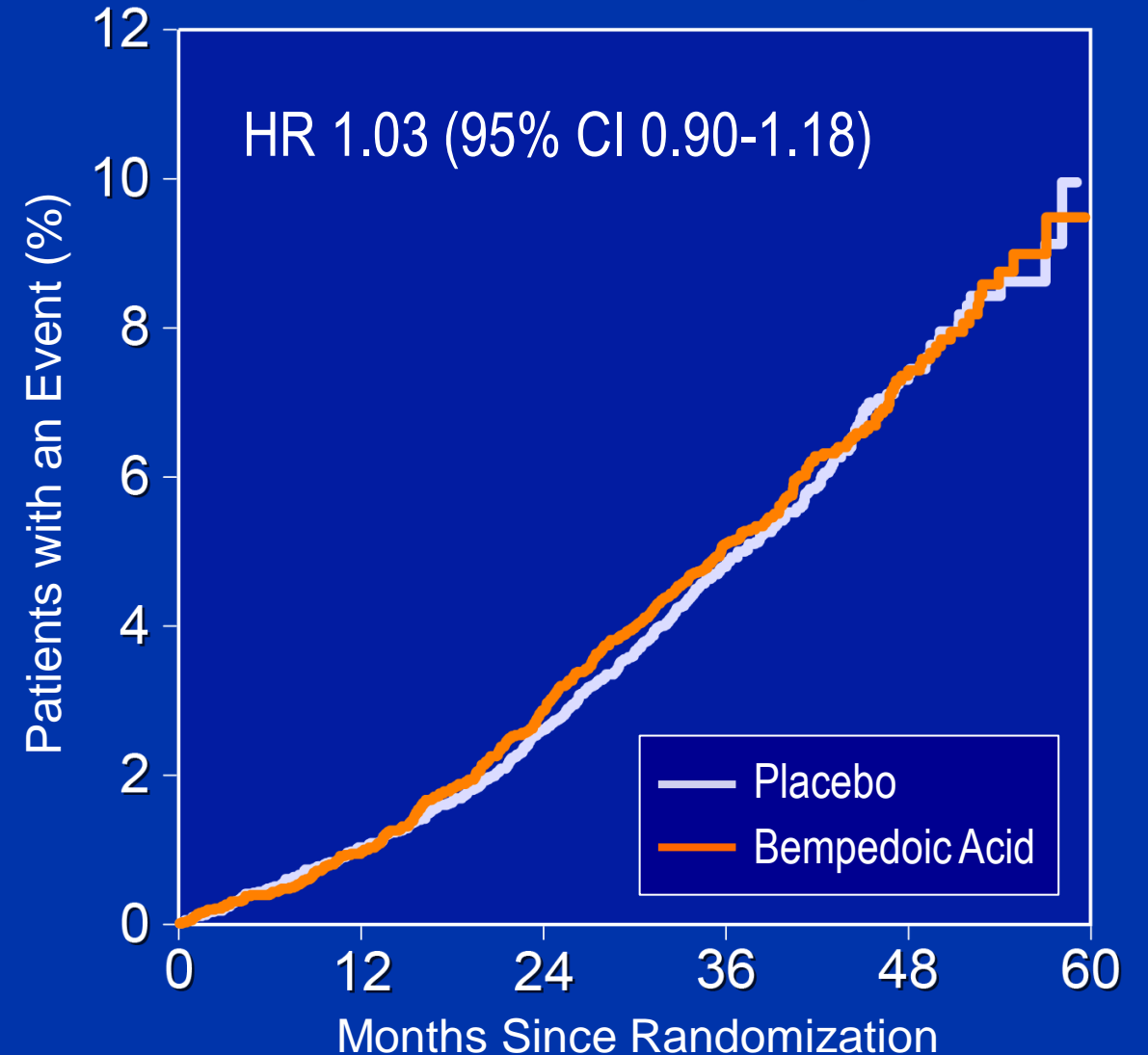


Effects of Trial Regimens on Mortality End Points

Cardiovascular Death



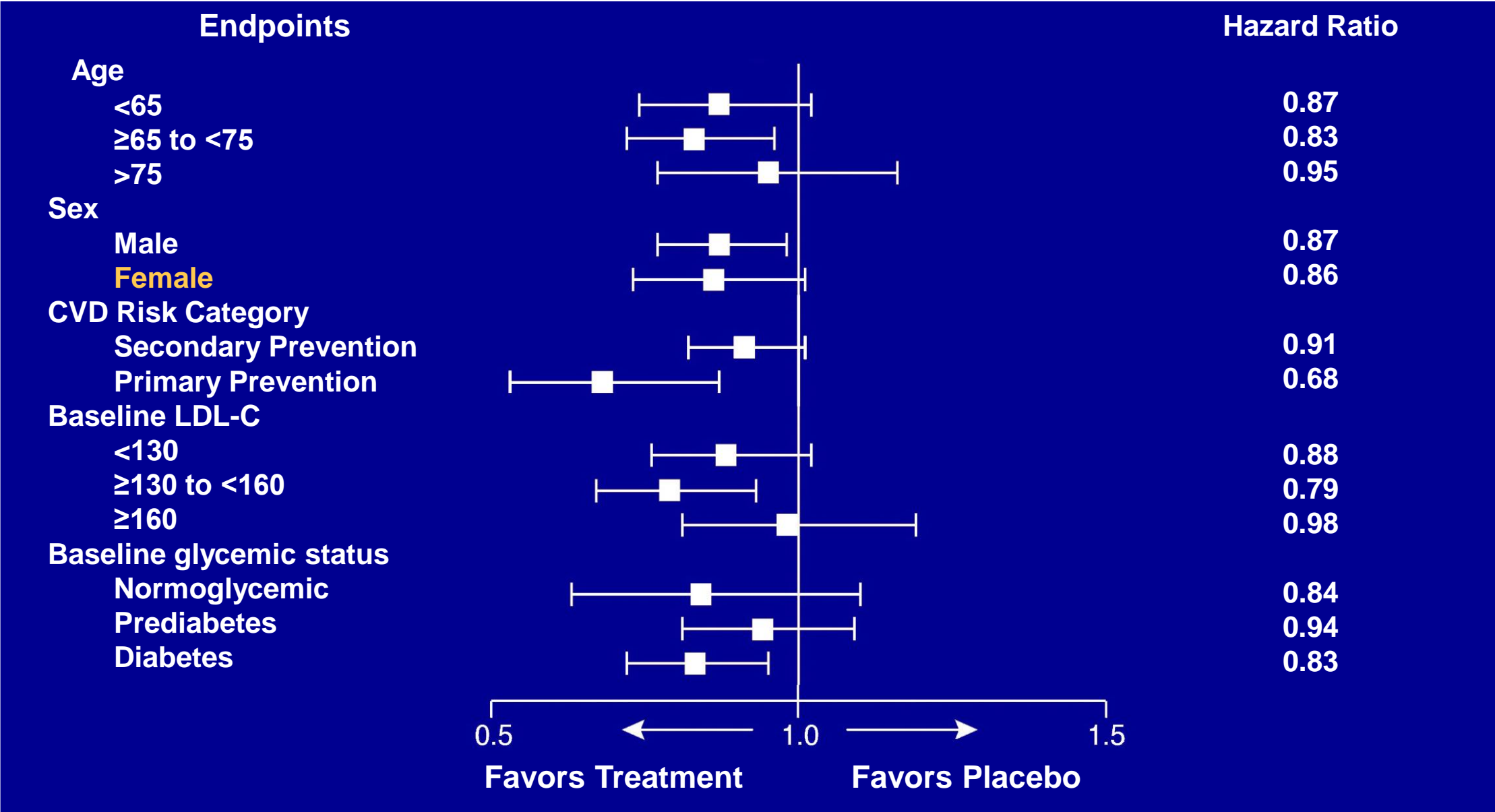
All-cause Mortality



Investigator-Reported Adverse Effects

Characteristic	Bempedoic Acid N=7001	Placebo N=6964
Serious Treatment Emergent Adverse event	25.2%	24.9%
Adverse event leading to drug discontinuation	10.8%	10.4%
Any muscle disorder	15.0%	15.4%
New onset diabetes	16.1%	17.1%
Elevated hepatic enzymes	4.5%	3.0%
Prespecified renal events	11.5%	8.6%
Gout	3.1%	2.1%
Cholelithiasis	2.2%	1.2%
Adjudicated tendon rupture	1.2%	0.9%

Primary MACE-4 End Point in Selected Subgroups



Limitations

- The trial enrolled only patients with documented statin intolerance. Effects in other populations were not studied.
- Addition of other therapies (including PCSK9 inhibitors) narrowed the LDL-C differences between bempedoic acid and placebo over time.
- The pandemic created challenges in achieving complete follow up, although full outcome data were available in 95.3% of patients and vital status determined in 99.4%.

Conclusions

- Bempedoic acid was well-tolerated in a mixed population of primary and secondary prevention patients unable or unwilling to take statins
- Bempedoic acid lowered LDL-C by 21.7% and hsCRP by 22.2% with small increases in the incidence of gout and cholelithiasis.
- The primary end point, 4-component MACE was reduced 13%, 3-component MACE 15%, myocardial infarction 23% and coronary revascularization 19%.
- These findings establish bempedoic acid as an effective approach to reduce major cardiovascular events in statin intolerant patients.



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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[☆]

A Final Thought

Management of patients unable or unwilling to take statins represents a challenging and frustrating clinical issue.

Regardless whether this problem represents the nocebo effect or actual intolerance, these high-risk patients need effective alternative therapies.

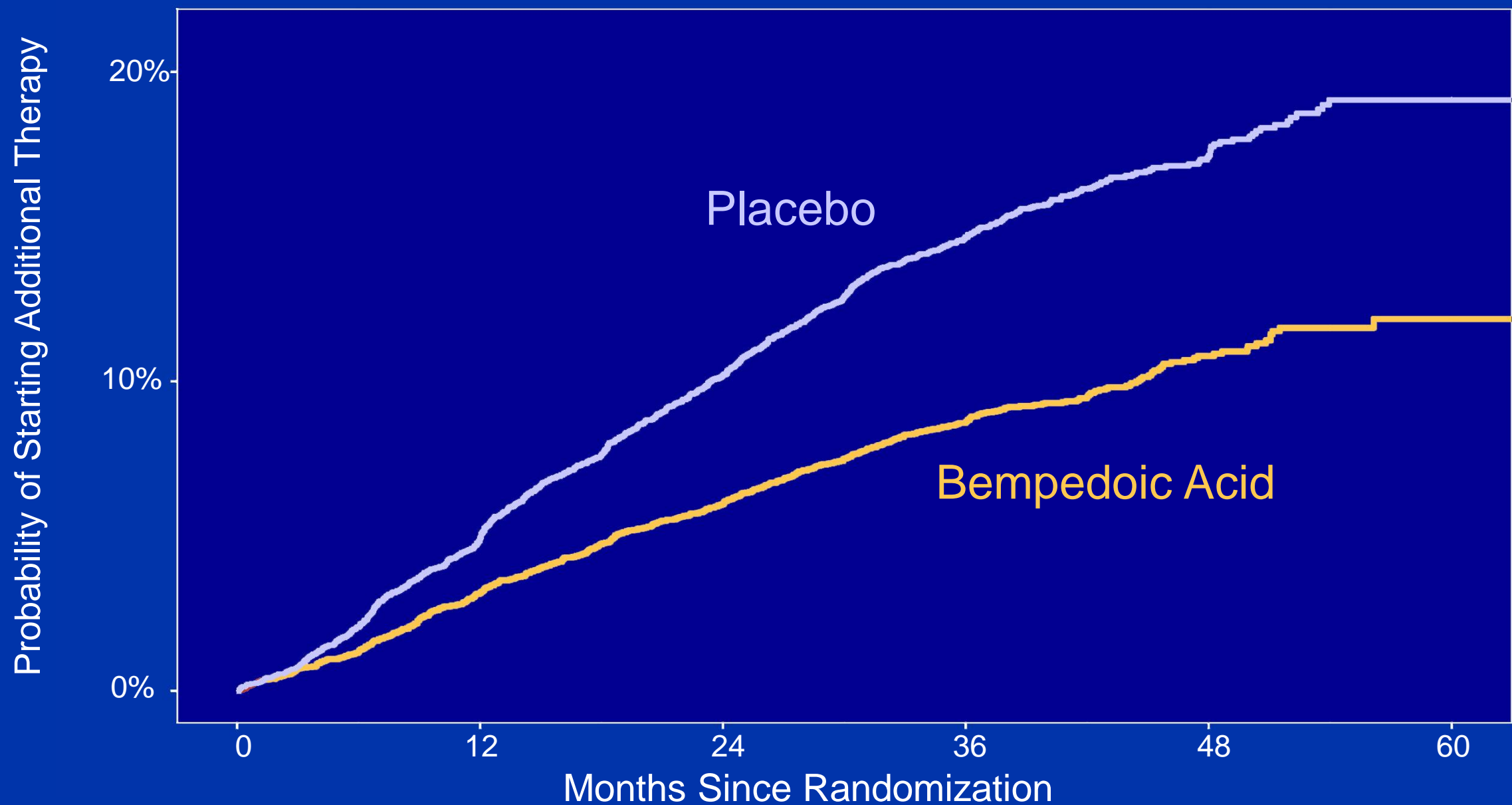
The CLEAR Outcomes trial provides a sound rationale for use of bempedoic acid to reduce major adverse cardiovascular outcomes in patients intolerant to statins.

Summary of All LMT Cross-ins During the Trial

LMT Category	Bempedoic Acid (N = 6992)	Placebo (N = 6978)
Any LMT	660 (9.4%)	1089 (15.6%)
Statins*	283 (4.0%)	456 (6.5%)
PCSK9 inhibitors -mAb	194 (2.8%)	306 (4.4%)
Selective Cholesterol Absorption Inhibitors (Ezetimibe)	189 (2.7%)	382 (5.5%)
Fibrates	72 (1.0%)	91 (1.3%)
Bile Acid Sequestrants	11 (0.2%)	17 (0.2%)
Bempedoic Acid	11 (0.2%)	10 (0.1%)
Fixed Dose Combination: Bempedoic Acid + Ezetimibe	6 (0.1%)	3 (<0.1%)
PCSK9-siRNA	4 (0.1%)	5 (0.1%)
Niacin derivatives	4 (0.1%)	6 (0.1%)

* At the end of the study <4% patients receiving a moderate or high intensity statin

Time to Cross-in to Additional Lipid Modifying Therapy



CTTC End Point Calculation

Bempedoic Acid (N=6992), n (%)	Placebo (N=6978), n (%)	HR	P-value
703 (10.1)	816 (11.7)	0.85 (0.77,0.94)	0.001

	Bempedoic Acid (N=6992)	Placebo (N=6978)
Baseline, n	6992	6978
Mean (SD)	139.0 (34.9)	139.0 (35.2)
Month 12, n	5977	5824
Mean (SD)	107.2 (37.8)	133.2 (41.4)
Change from baseline, LS Mean (SE)	-28.5 (0.42)	-2.47 (0.43)
Difference of LS Means (SE)	-26.1 (0.59) mg/dl (0.67 mmol/L)	

CTTC calculation = Expected HR for 0.67 mmol/L LDL-C reduction = **0.846**

Outcomes: Non-Statin LDL-C Lowering Therapies

	3-Component MACE	Nonfatal MI
Ezetimibe	0.90	0.87
Evolocumab	0.80	0.73 [†]
Alirocumab	0.86*	0.86
Bempedoic Acid	0.85	0.73

*Trial used all-cause mortality rather than CV death

[†]Fatal and nonfatal MI

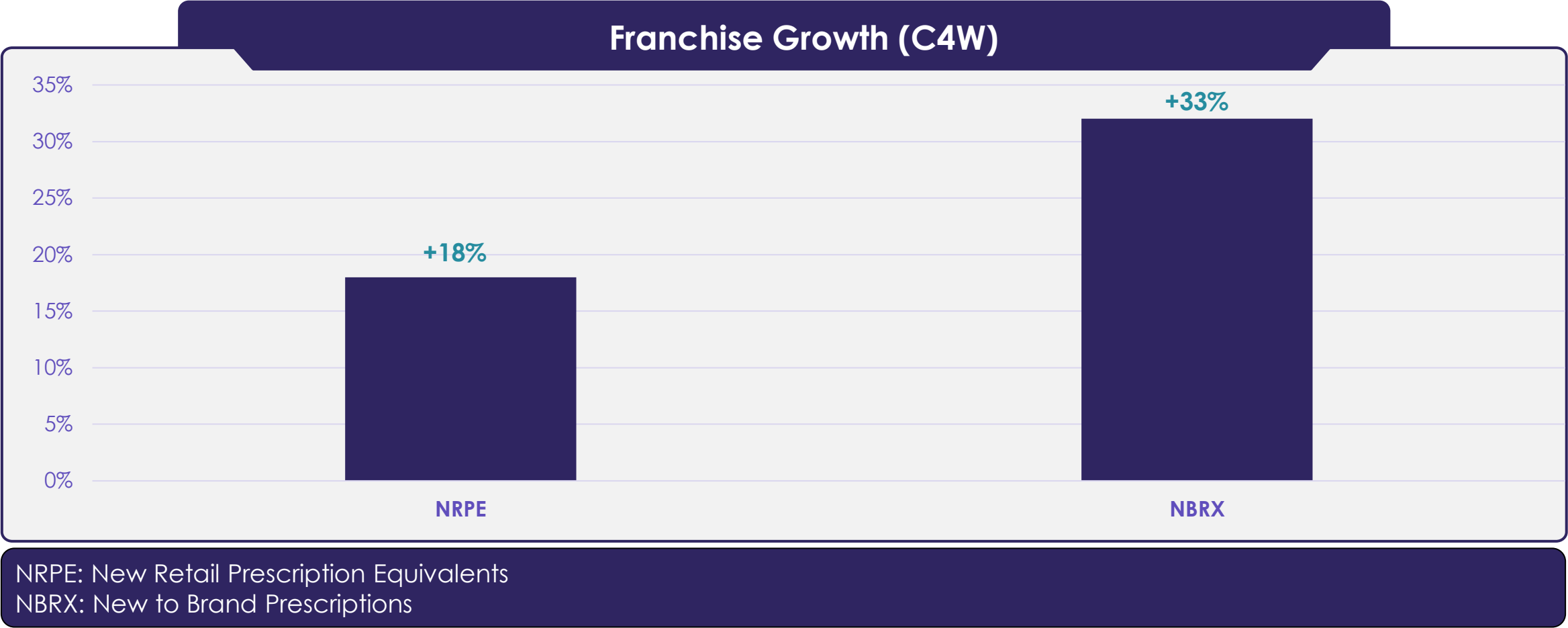


Commercial Update

Eric Warren, R.Ph.

Chief Commercial Officer

We Entered ACC 23 With Momentum, Demonstrating Robust Franchise Growth Across Key Metrics (NRPE and NBRX)



Symphony Health RX data through 2/17/23 (Combined NEXLIZET and NEXLETOL)



CLEAR Outcomes is the Catalyst for Exponential Growth

1

First Non-Statins LDL-C Lowering Agent to Demonstrate Clinical Outcomes Benefit in a combination of High-Risk Primary and Secondary Prevention Patients

2

Quantitative Market Research Validates the Significant Role NEXLIZET and NEXLETOL will Play in Clinical Practice

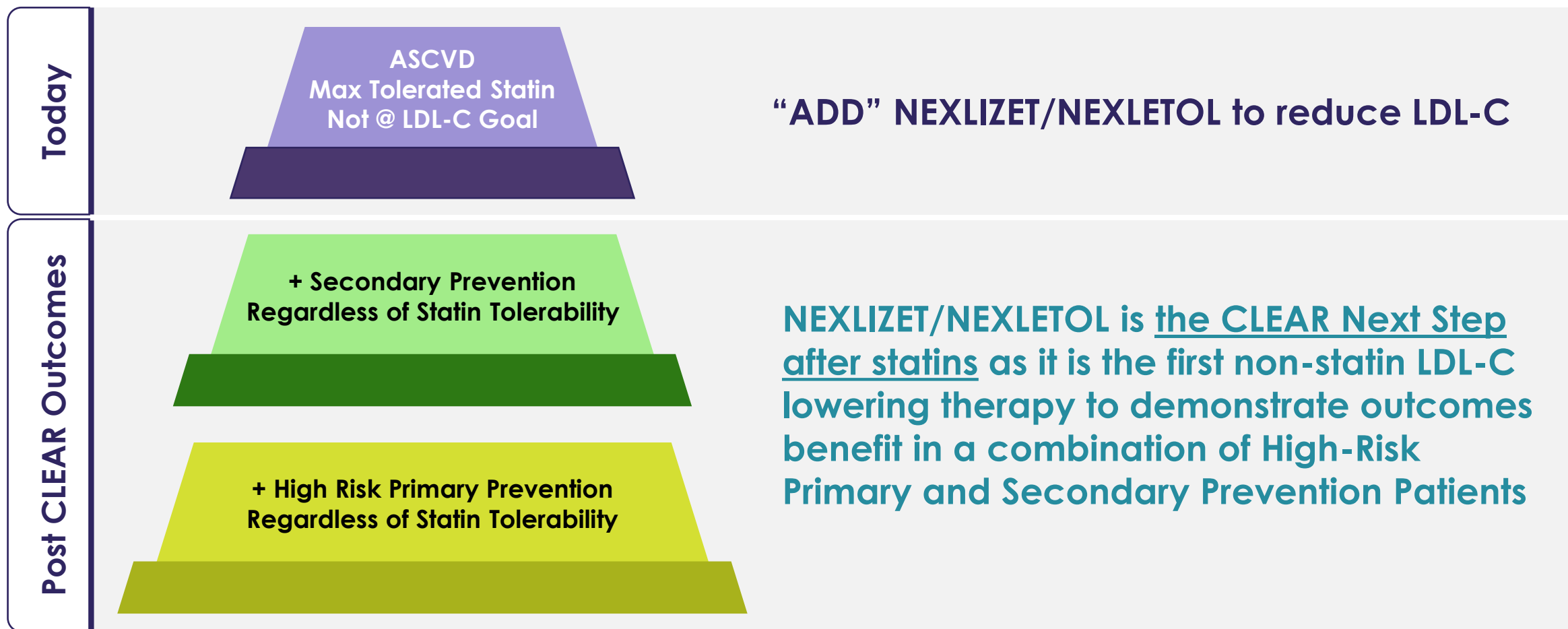
3

Commercial Activities will be Scaled to Realize Full-Potential

NEXLIZET/NEXLETOL is the CLEAR Next Step after Statins

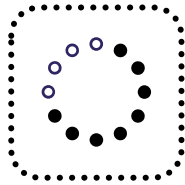
Enhanced Positioning Post CLEAR Outcomes

6x Increase in Addressable Patients by Removing Max Tolerated Statin and ASCVD Limitations



Quantitative Market Research Validates the Significant Role NEXLIZET and NEXLETOL will have as the CLEAR Next-Step after Statins

Methodology:



- 250 HCPs (CDs, PCPs, Endos) Including both prescribers and non-prescribers of NEXLIZET/NEXLETOL
- 30-minute conjoint analysis assessing market share using ranges of outcomes across key primary and secondary endpoints

Results:



Totality of evidence drives exponential increase in market share

- MACE-4 RRR ranging between 11-17% resulted in ~equivalent and significant share increases
- 95% of clinicians said they would now prescribe NEXLIZET or NEXLETOL “Next” after a statin
- Clinicians will increase prescribing for both primary and secondary prevention patients
- NEXLIZET and NEXLETOL will take share across a range on non-statins with ezetimibe (market leading non-statin) the #1 source of business

Commercial Activities Underway To Ensure NEXLIZET and NEXLETOL are the CLEAR Next Step after Statins

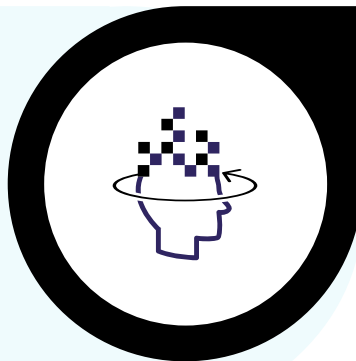
**HCP Segmentation and
Field Sales Force Sizing**
(Q1 2023)



**Promotional Message
Updates Leveraging
Current Label**
(Q2 2023)



**Prepare CLEAR Launch
Campaign and
Promotional Messaging**
(Q2 2023 - Q1 2024)



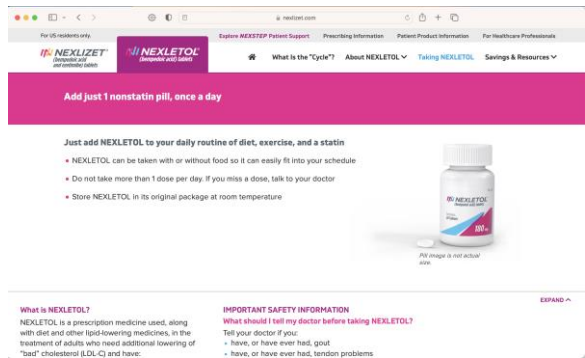
**Field Sales Force
Expansion in Advance of
Label Change**
(Q4 2023)



ACC 23: Late Breaker Has Generated Significant Increase in Brand Awareness

1426% ↑

PATIENT WEBSITE ACTIVITY





Payer Update

BJ Swartz

Chief Strategy Officer

Place in Therapy and Formulary Positioning

Appropriate utilization criteria for NEXLETOL and NEXLIZET is **NEXT** for patients using statins or history of statin intolerance, and stepped before PCSK9is, as a non-specialty oral product with proven outcomes data.

Current Payer Coverage

- 90% Commercial and 34% Medicare
- Bempedoic acid placed **NEXT** as an add-on treatment for high-risk (ASCVD) patients already on maximally tolerated statin therapy who need additional LDL-C lowering to achieve treatment goals
- Immediately post ACC, 30 Payer clinical meetings scheduled

With CLEAR Outcomes... Reduced burden of PAs

- Bempedoic acid becomes the only oral non-statin therapy to demonstrate CV risk reduction in both primary and secondary prevention
- Bempedoic acid provides good value by preventing CV events in high-risk patients and patients with established ASCVD while reducing the need for expensive, injectable therapies (PCSK9is)
- Anticipate rapid uptake of Medicare coverage to 70%



FY 2023 Financial Guidance

Ben Halladay

Chief Financial Officer

Financial Strength to Deliver Growth

Cash runway sufficient beyond CLEAR Outcomes through the end of 2023

\$167M

2022 Cash, Cash Equivalents & Investment Securities Available-for-Sale

\$300M

Expected Milestone Payment for European Label Expansion

Key Financial Data

FY 2023 R&D Guidance	\$100-110 Million
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FY 2023 SG&A Guidance	\$125-135 Million
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FY 2023 Op Ex Guidance ¹	\$225-245 Million
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Q4 2022 Common Shares Outstanding ²	74.6 Million
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1. Includes \$25M of non-cash stock-based compensation expense

2. After accounting for 2.0 million treasury shares to be purchased in the \$50M prepaid forward transaction as part of the November 2020 convertible debt financing



Key Takeaways

Sheldon Koenig

President & CEO

Key Takeaways

1

We have a unique and successful outcome study in a large therapeutic category that demonstrates the benefits of bempedoic acid, the active ingredient in NEXLETOL® & NEXLIZET®

2

We are poised for a major inflection in sales and prescriptions and are targeting blockbuster status

3

Based on the robustness of the CLEAR Outcomes data, we believe we would be entitled to receive \$300 million in milestone payments from collaborative partners upon inclusion of cardiovascular risk reduction data in the European label and up to \$140 million upon other regulatory milestones



Thank you



Q & A



Important Safety Information

Esperion Confidential. Do not copy. For internal use only. Not for use in promotion.

NEXLETOL[®] Safety Profile

- Contraindications: None
- Warnings and Precautions:
 - Hyperuricemia: NEXLETOL may increase blood uric acid levels, and may lead to the development of gout, especially in patients with a history of gout.
 - Tendon Rupture: NEXLETOL is associated with an increased risk of tendon rupture.
- Avoid concomitant use with simvastatin (>20 mg/day) or pravastatin (>40 mg/day) due to increased risk of adverse events.
- Most common adverse reactions in $\geq 2\%$ of patients taking NEXLETOL and more frequently than placebo:
 - Upper respiratory tract infection, muscle spasms, hyperuricemia, back pain, abdominal pain or discomfort, bronchitis, pain in extremity, anemia, and elevated liver enzymes
- Adverse events reported less frequently but still more often than in placebo included benign prostatic hyperplasia and atrial fibrillation

This summary does not reflect the full safety profile – please see <https://pi.esperion.com/nexletol/nexletol-pi.pdf>

NEXLIZET[®] Safety Profile

- Contraindication: Known hypersensitivity to ezetimibe tablets
- Warnings and Precautions:
 - Hyperuricemia: Bempedoic acid may increase blood uric acid levels, and may lead to the development of gout, especially in patients with a history of gout.
 - Tendon Rupture: Bempedoic acid is associated with an increased risk of tendon rupture.
- Avoid concomitant use with simvastatin (>20 mg/day) or pravastatin (>40 mg/day). Monitor cyclosporine concentrations with cyclosporine. If cholelithiasis is suspected in a patient receiving fenofibrate, consider alternative lipid-lowering therapy.
- Most common adverse reactions in >2% of patients taking NEXLIZET and more frequently than placebo:
 - Upper respiratory tract infection, muscle spasms, hyperuricemia, back pain, abdominal pain or discomfort, bronchitis, pain in extremity, anemia, elevated liver enzymes, diarrhea, fatigue, influenza, sinusitis, and arthralgia
- Adverse events reported less frequently but still more often than in placebo included benign prostatic hyperplasia and atrial fibrillation

This summary does not reflect the full safety profile - see <https://pi.esperion.com/nexlize/nexlize-pi.pdf>