Effect of Evolocumab on Atherogenic Lipoproteins During the Peri- and Early Postinfarction Period: A Placebo-Controlled, Randomized Trial *Results From the EVACS Study*

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EVACS = Evolocumab in Acute Coronary Syndrome.

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Introduction

- Patients with acute coronary syndromes (ACS) are at increased risk of recurrent cardiovascular events[1]
- Studies have shown that earlier and more intensive LDL-C lowering provides greater protection[2,3,4,5]
- Achieving AHA/ACC and ESC guideline recommended LDL-C (< 70 mg/dL [< 1.8 mmol/L] and < 55 mg/dL [< 1.4 mmol/L] for secondary prevention in high-risk patients such as those with ACS, is challenging.[6,7]
- An additional option on top of high-intensity statins for more rapid lowering of LDL-C during the peri- and early post-ACS period is PCSK9 inhibition[8]
- The EVACS trial (**EV**olocumab in **A**cute **C**oronary **S**yndrome) aimed to evaluate the effect of evolocumab on atherogenic lipoproteins during the peri- and early postinfarction period in patients with ACS*[7]

*Type 1 NSTEMI (spontaneous atherothrombotic)

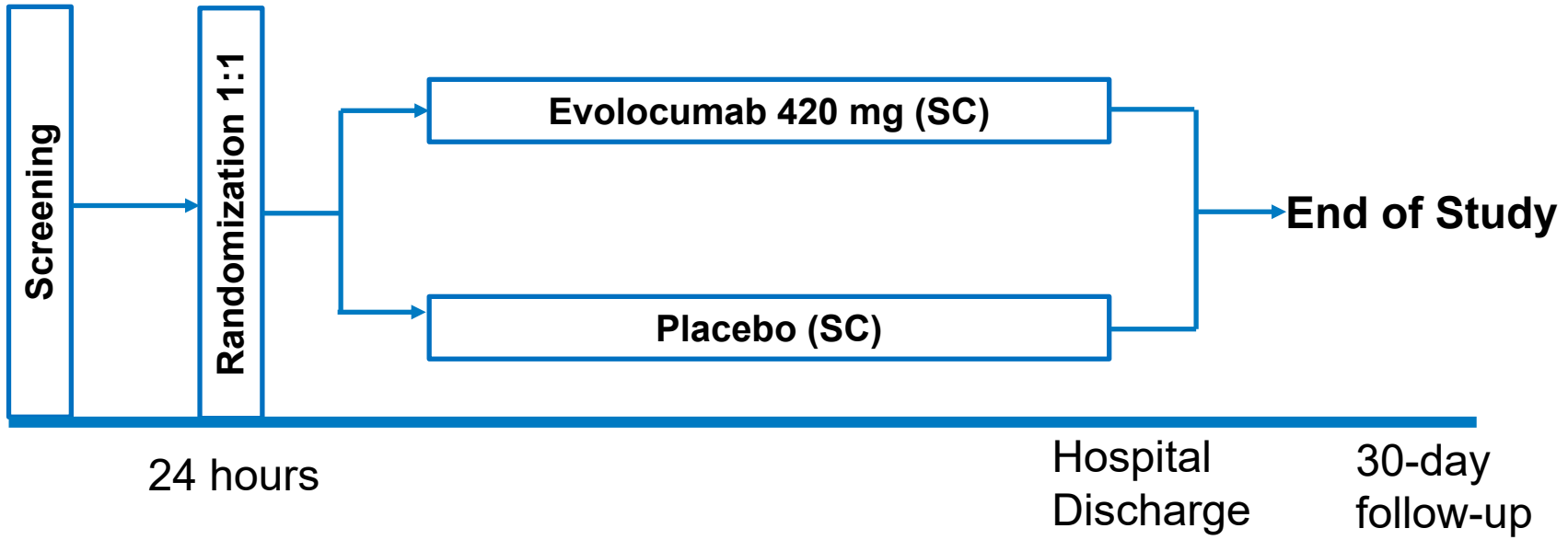
ACC = American College of Cardiology; ACS = acute coronary syndrome; AHA = American Heart Association; ESC = European Society of Cardiology; EVACS = Evolocumab in Acute Coronary Syndrome; LDL-C = low-density lipoprotein cholesterol; PCSK9 = proprotein convertase subtilisin/kexin type 9; SC = subcutaneous.

1. Jernberg T, et al. Eur Heart J. 2015;36:1163-1170. 2. Cannon CP, et al. *N Engl J Med*. 2015;372:2387-2397. 3. Cannon CP, et al. *N Engl J Med*. 2004;350:1495-1504. 4. de Lemos JA, et al. *JAMA*. 2004;292;1307-1316. 5. Schwartz GG, et al. *JAMA*. 2001;285:1711-1718. 6. Grundy SM, et al. *Circulation*. 2019;139(25):e1082-e1143. 7. Leucker TM, et al. *Circulation.* 2020;142:419-421. 8. Schwartz GG, et al. *N Eng J Med.* 2018;379:2097-2107.

EVACS: A Double-Blind, 1:1 Randomized, Placebo-controlled Trial

Eligibility Criteria:
- Type 1 Non-STEMI
- Troponin I ≥ 5 ng/mL

Study Endpoints:
Primary: Change in LDL-C at Day 30
Secondary: Change in other atherogenic lipoproteins



- 57 patients met eligibility criteria and were included in the study
- Patients were randomized (1:1 ratio) to receive a single dose of either evolocumab SC 420 mg or matching placebo within 24 hours of presentation
- All participants received high-intensity statins unless contraindicated and were treated per current ACS guidelines

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Other Than Differences in Sex Distribution, Baseline Characteristics Were Similar

Baseline Characteristics	Placebo (N=27)	Evolocumab (N=30)	P-value
Age (years), mean±SD	56.6 ±12.7	53.9±13.4	0.46
Male gender, n (%)	11 (40.7)	22 (73.3)	0.03
African American, n (%)	9 (33.3)	6 (20)	0.40
BMI (kg/m^2), mean±SD	28.5±7.0	27.4±7.3	0.56
Diabetes mellitus, n (%)	6 (22.2)	14 (46.7)	0.10
Hypertension, n (%)	23 (85.2)	21 (70)	0.29
Active smoking, n (%)	6 (22.2)	7 (23.3)	1.00
Previous myocardial infarction, n (%)	7 (26)	14 (46.7)	0.18
History of stroke, n (%)	4 (14.8)	1 (3.3)	0.29
Prior statin treatment, n (%)	14 (51.9)	20 (66.7)	0.39
Low- or moderate-intensity statin	6 (22.2)	8 (26.7)	0.94
High-intensity statin	8 (29.6)	12 (40)	0.59
Ezetimibe treatment, n (%)	0 (0)	0 (0)	0.69
LDL-C (mg/dL), mean±SD	89.6 ± 41.4	91.5 ± 34.8	0.85
Non-HDL-C (mg/dL), mean±SD	110.0 ± 44.7	111.7 ±38.5	0.88
ApoB (mg/dL), mean±SD	80.7±24.0	71.5±20.2	0.14

Lipid-lowering therapy and intensity at baseline were similar between the study groups

ApoB = apolipoprotein B; BMI = body mass index; LDL-C = low-density lipoprotein cholesterol; Non-HDL-C = non-high-density lipoprotein cholesterol; SD = standard deviation.

Leucker TM, et al. *Circulation.* 2020;142:419-421. (Table included with permission from Dr. Thorsten Leucker, August 12, 2020. To be presented at ESC 2020 – The Digital Experience. August 29 – September 1, 2020. LDL-C Management in ACS: Lower is Better But Is Earlier Better?)

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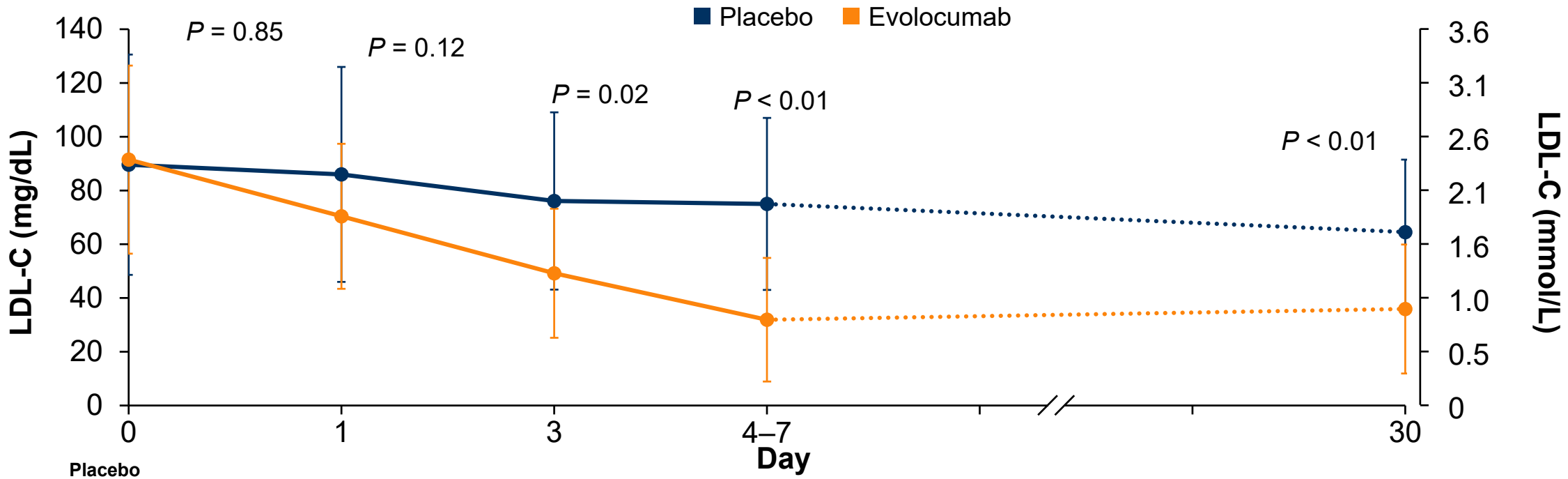
LDL-C Levels Declined as Early as Day 1 After Administration Of Evolocumab and Were Significantly Reduced Compared to Placebo By Day 3



Placebo					
mg/dL	89.6 ± 41	86.0 ± 40	76.1 ± 33	75.0 ± 32	64.5 ± 27
mmol/L	2.3 ± 1.1	2.2 ± 1.0	2.0 ± 0.9	1.9 ± 0.8	1.7 ± 0.7
Evolocumab					
mg/dL	91.5 ± 35	70.4 ± 27	49.2 ± 24	31.9 ± 23	35.9 ± 24
mmol/L	2.4 ± 0.9	1.8 ± 0.7	1.3 ± 0.6	0.8 ± 0.6	0.9 ± 0.6

Evolocumab, added to statin therapy, significantly reduced LDL-C levels throughout hospitalization and the 30-day follow-up in comparison with the placebo group (statin alone) (35.9 ± 24mg/dL (0.9±0.6 mmol/L) evolocumab vs. 64.5 ± 27 mg/dL (1.7±0.7 mmol/L); *P* < 0.01).

The number of patients assessed at the different time points are as follows: Baseline, 57 (evolocumab n = 30; placebo n = 27); day 1, 51 (evolocumab n = 26; placebo n = 25); day 3, 30 (evolocumab n = 16; placebo n = 14); day 4 to 7, 23 (evolocumab n = 15; placebo n = 8); day 30, 57 (evolocumab n = 30; placebo n = 27).
LDL-C = low-density lipoprotein cholesterol.

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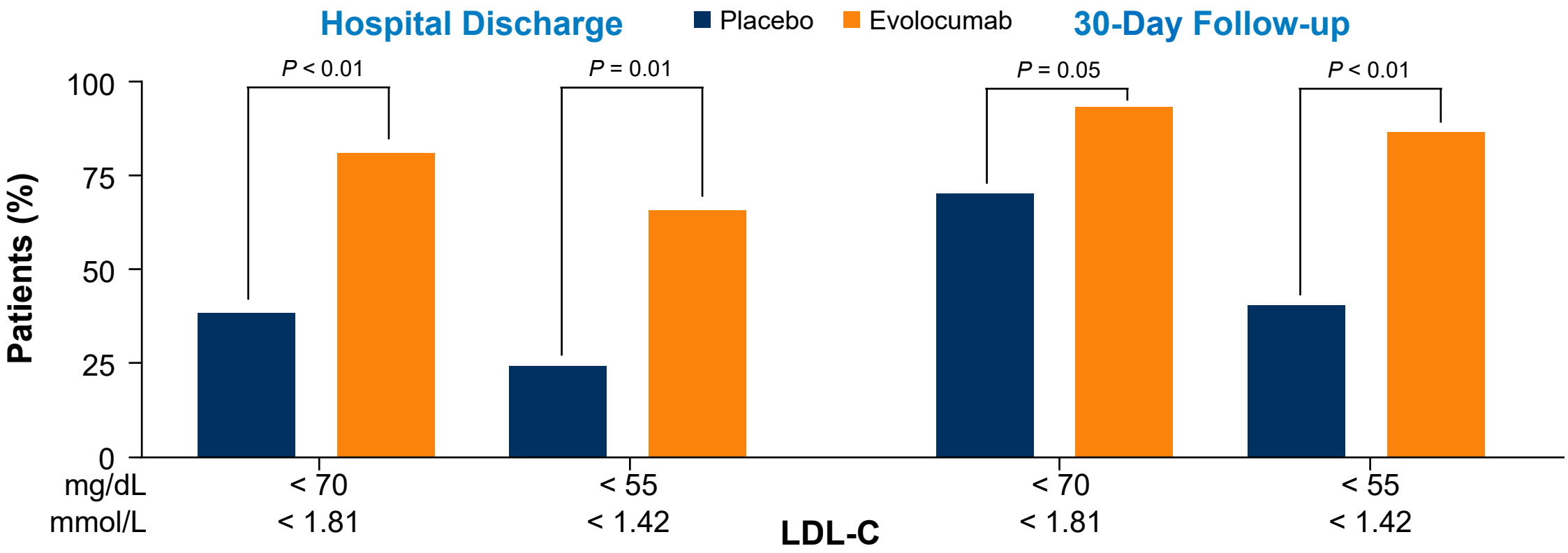
Significantly More Patients Treated With Evolocumab Achieved AHA/ACC and ESC LDL-C Guideline Recommendations At Hospital Discharge & At 30-Day Follow-Up



At hospital discharge[a] (~Day 4)[a], 80.8% and 65.4%, respectively, of evolocumab-treated patients achieved 2018 AHA/ACC and 2019 ESC guideline LDL-C recommendations compared with 38.1% and 23.8%, respectively, of placebo-treated patients

[a]The mean discharge day was 4±2 days. Discharge values were obtained within 24 hours of discharge (evolocumab n = 26; placebo n = 21).
ACC = American College of Cardiology; AHA = American Heart Association; ESC = European Society of Cardiology; LDL-C = low-density lipoprotein cholesterol.

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Incidence of AEs and SAEs Were Similar Between the Treatment Groups

	Evolocumab (n)	Placebo (n)
Any AE	10	12
Serious AE	2	6

AE = adverse event. SAE = serious adverse event.

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Evolocumab Rapidly and Significantly Reduced LDL-C in the Acute ACS Setting and Maintained This Reduction for 30 Days

- EVACS, a randomized clinical trial assessing the impact of evolocumab on peri- and early post-infarction levels of atherogenic lipoproteins in patients with ACS, demonstrated that treatment with evolocumab in the hospital early after ACS resulted in rapid reduction of LDL-C in just 24 hours compared to baseline
- Evolocumab, added to statin therapy, significantly reduced LDL-C levels by Day 3 after ACS and continued throughout hospitalization and the 30-day follow-up in comparison with the placebo group (statin alone) (35.9±24mg/dL (0.9±0.6 mmol/L) evolocumab vs. 64.5±27mg/dL (1.7±0.7 mmol/L); $P < 0.01$)
- Incidence of adverse events and serious adverse events were similar between the treatment groups
- At hospital discharge (~4 days) significantly more patients treated with evolocumab and a statin achieved AHA/ACC and ESC guideline LDL-C recommendations and were maintained at 30 days

ACC = American College of Cardiology; ACS = acute coronary syndrome; AHA = American Heart Association; ESC = European Society of Cardiology; EVACS = Evolocumab in Acute Coronary Syndrome; LDL-C = low-density lipoprotein cholesterol.

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EVACS Back-Up Slides

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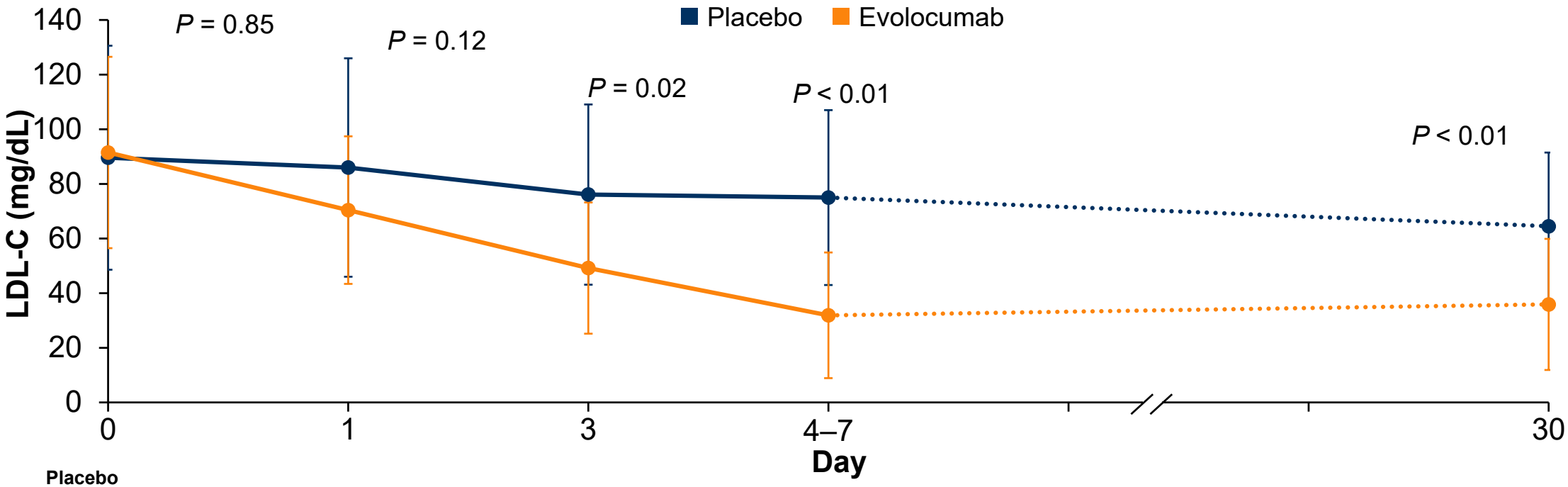

	0	1	3	4–7	30
Placebo mg/dL	89.6 ± 41	86.0 ± 40	76.1 ± 33	75.0 ± 32	64.5 ± 27
Evolucumab mg/dL	91.5 ± 35	70.4 ± 27	49.2 ± 24	31.9 ± 23	35.9 ± 24

Evolocumab, added to statin therapy, significantly reduced LDL-C levels throughout hospitalization and the 30-day follow-up in comparison with the placebo group (statin alone) (35.9±24mg/dL evolocumab vs. 64.5±27 mg/dL; *P* < 0.01).

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LDL-C = low-density lipoprotein cholesterol; SD = standard deviation.

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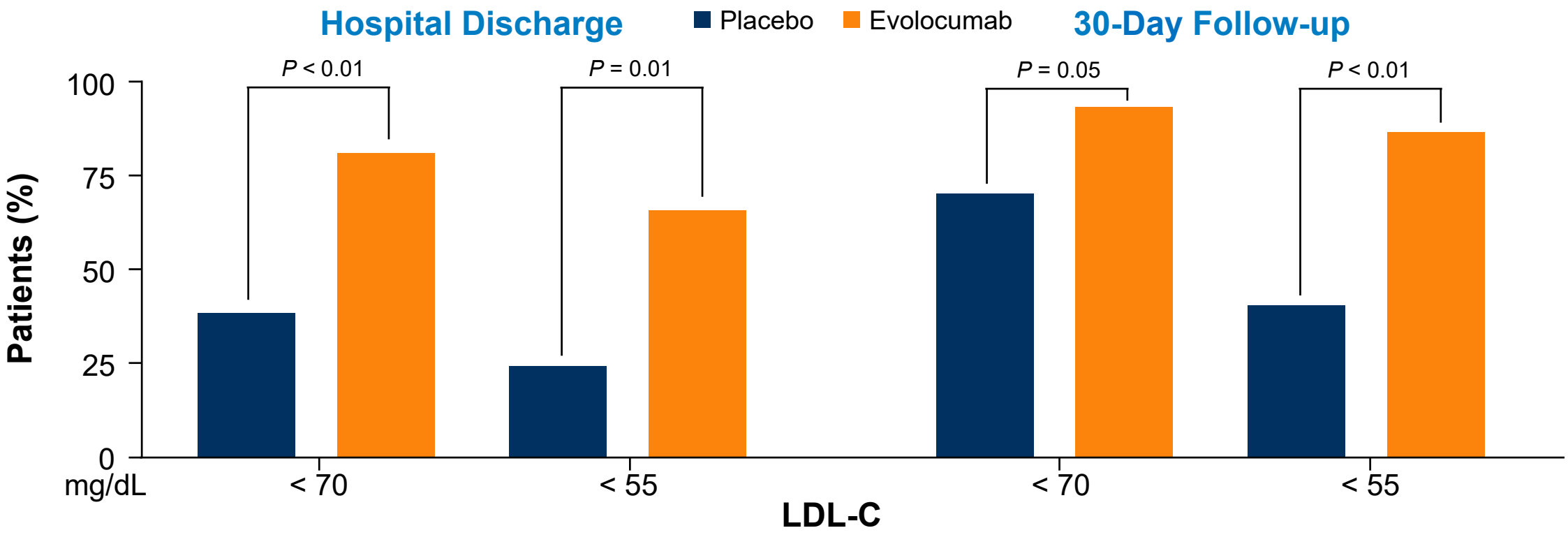
Significantly More Patients Treated With Evolocumab Achieved AHA/ACC and ESC LDL-C Guideline Recommendations At Hospital Discharge & At 30-Day Follow-Up



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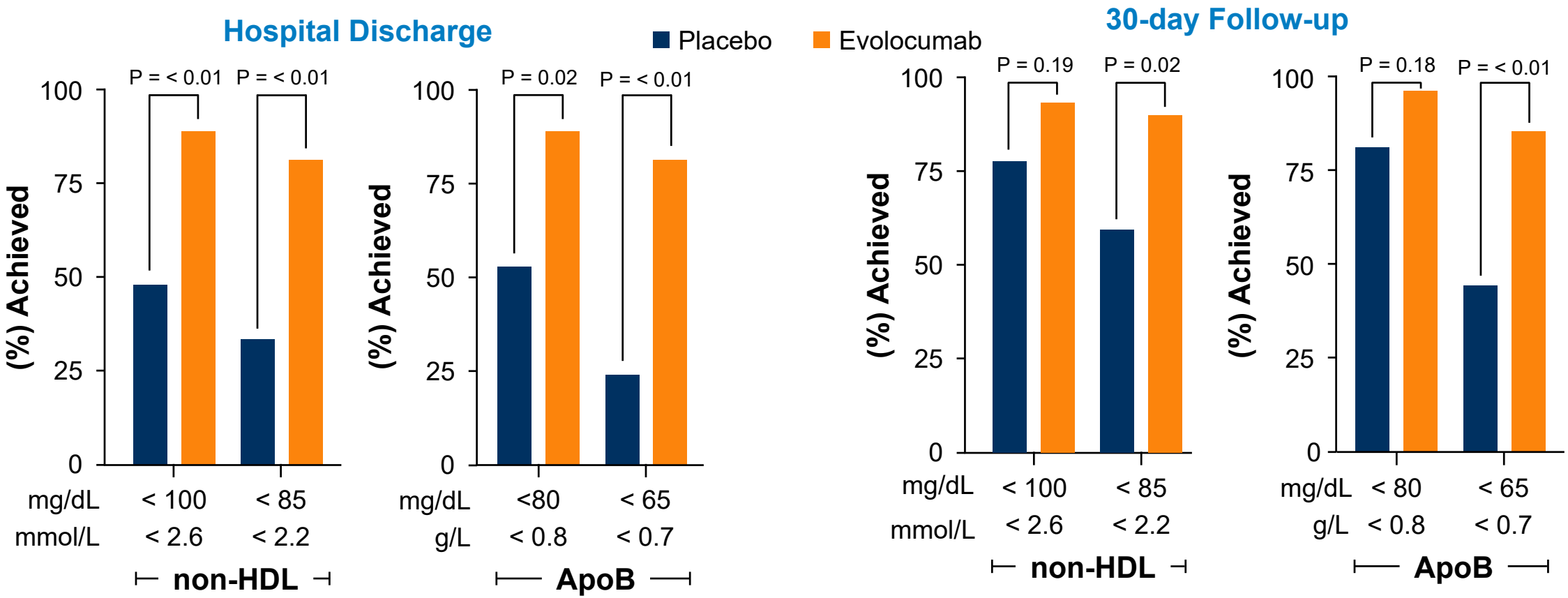
Evolocumab Significantly Reduced non–HDL-C and ApoB Levels at Hospital Discharge and 30-Day Follow-up



At hospital discharge[a] (~ Day 4) and 30-day follow-up, a greater percentage of evolocumab-treated patients had non–HDL-C and ApoB levels at or below 2018 AHA/ACC- and 2019 ESC-recommended target levels than placebo-treated patients

[a]The mean discharge day was 4±2 days. Discharge values were obtained within 24 hours of discharge (evolocumab n = 26; placebo n = 21).
ACC = American College of Cardiology; AHA = American Heart Association; ApoB = apoplipoprotein B; ESC = European Society of Cardiology; HDL-C = high-density lipoprotein cholesterol.

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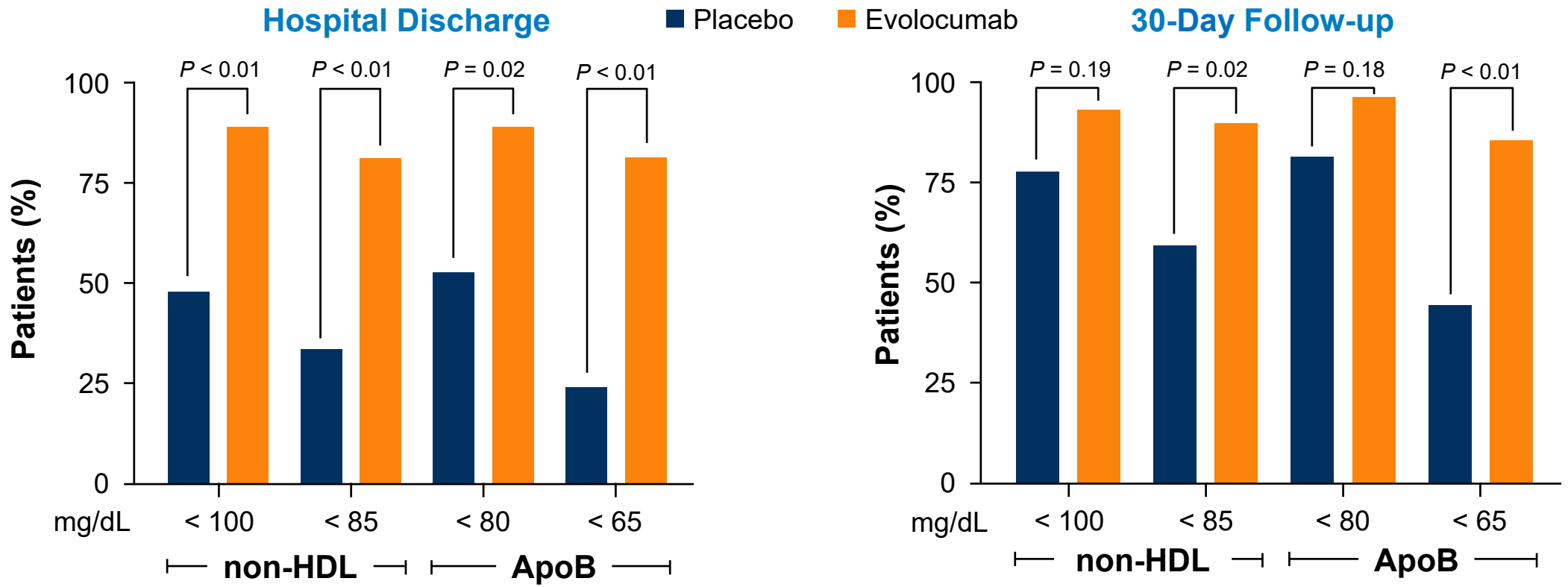
Evolocumab Significantly Reduced non–HDL-C and ApoB Levels at Hospital Discharge and 30-Day Follow-up



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