Effects of Routine Early Treatment with PCSK-9 Inhibitor in Patients Undergoing Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction: A randomized, double-blind, sham-controlled trial

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Background

- In patients with STEMI, early initiation of high intensity statin therapy, regardless of baseline LDL level is standard practice worldwide.
- The greater the reduction in LDL with statins, the lower the risk, with no apparent lower limit beyond which a benefit is not observed. Yet, a significant proportion of STEMI patients never achieve optimal LDL levels with statins
- PCSK9 inhibitors further reduce LDL and events but have been not studied when given acutely nor as routine treatment
- Whether a simplified regimen of initiating PCSK9 inhibitor *routinely* in the acute setting of STEMI on top of high intensity statins would add additional benefit by further reducing LDL-cholesterol levels in a much wider population of patients is unknown.
- On a population level, such an approach would be expected to substantially reduce the number of major cardiovascular events in this high-risk population.

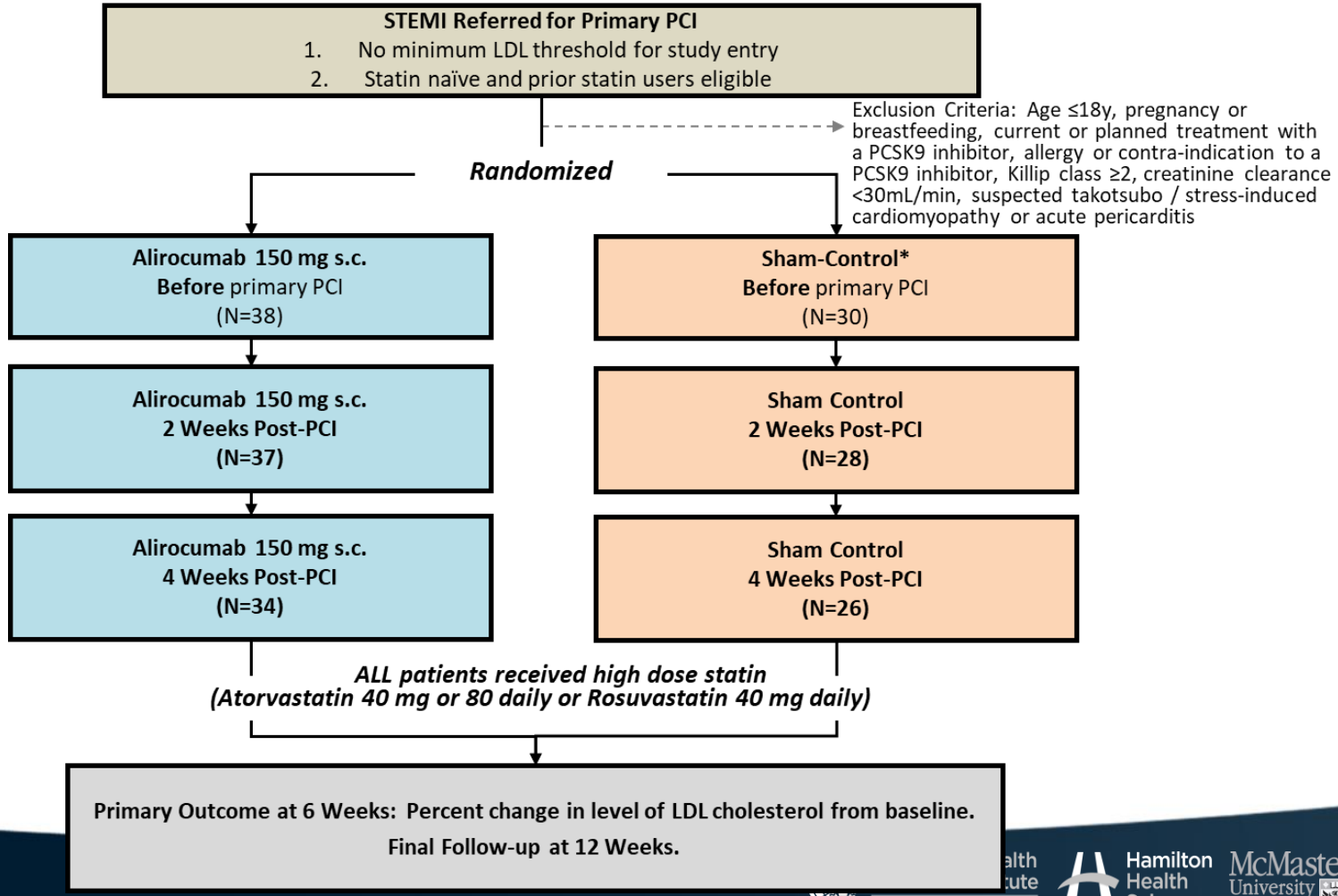
Objectives

EPIC-STEMI was designed to evaluate the routine, early administration of PCSK9 inhibitor, regardless of baseline LDL levels or prior statin use, in order to determine:

1. The degree of LDL reduction that might be expected with this approach
2. The time course of LDL lowering during the acute period after STEMI
3. The overall feasibility of this approach.

EPIC STEMI

Design Flow



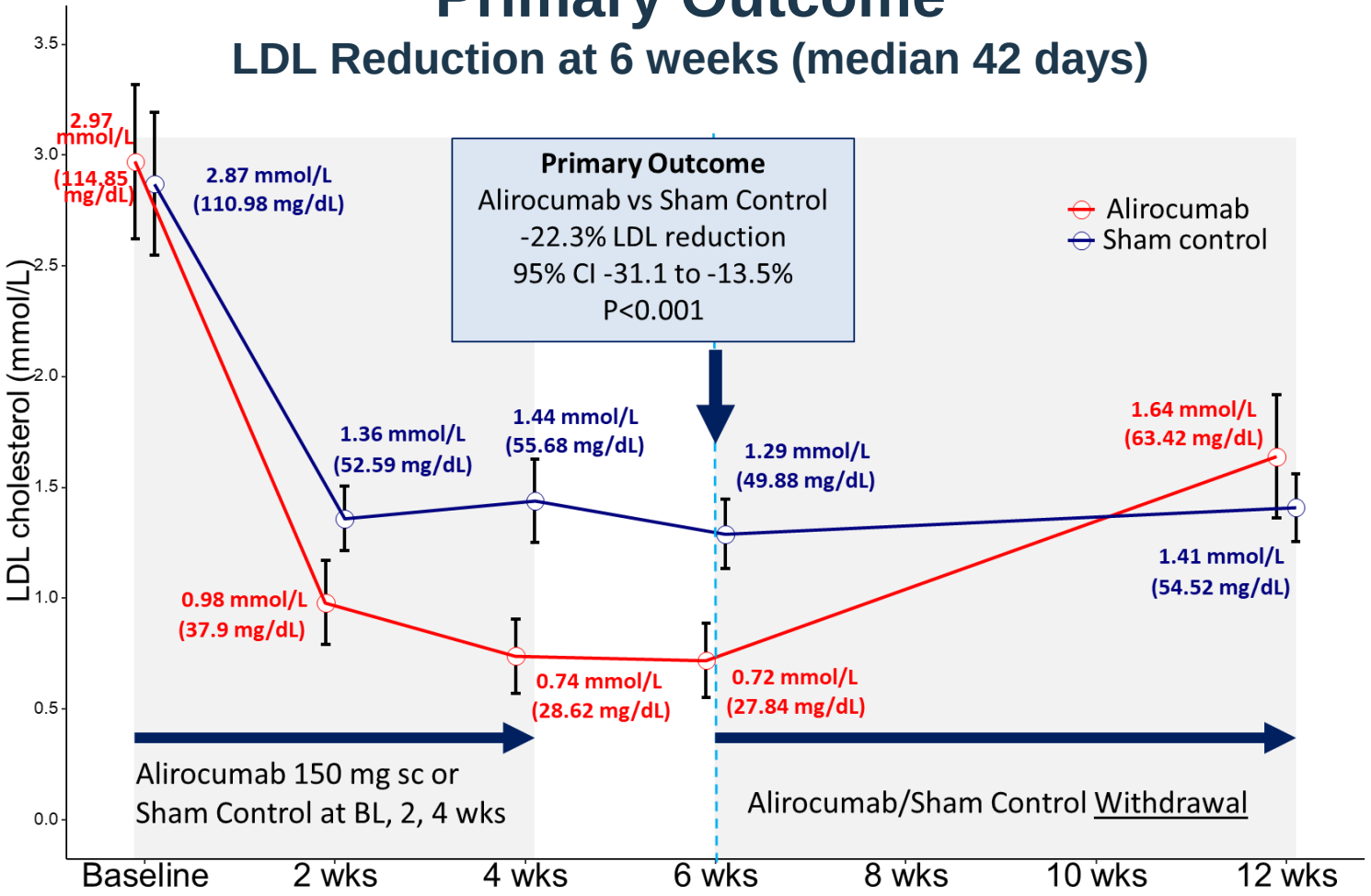
Baseline Characteristics

Median follow-up 45 days

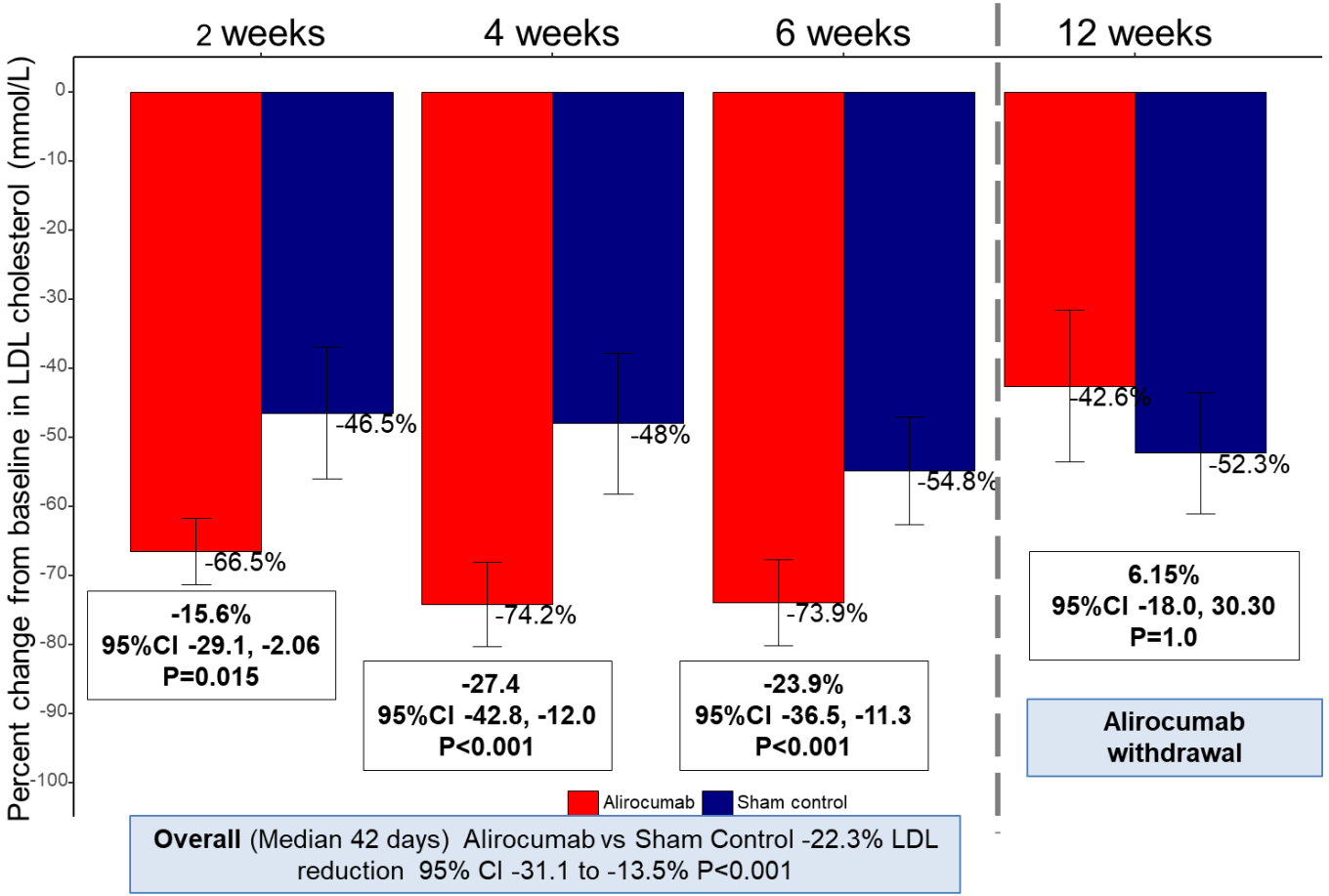
	Alirocumab N=38	Sham-Control N=30
Age (year)	61.37 (11.04)	63.63 (10.38)
Sex (male) - no.(%)	27 (71.05)	28 (93.33)
Medical History		
Diabetes - no.(%)	5 (13.16)	1 (3.33)
Prior myocardial infarction - no.(%)	3 (7.89)	3 (10.00)
Current smoker - no.(%)	16 (42.11)	7 (23.33)
Hypertension - no.(%)	17 (44.74)	13 (43.33)
Dyslipidemia - no.(%)	13 (34.21)	12 (40.00)
Prior stroke - no.(%)	1 (2.63)	0 (0.00)
Time from symptom onset to primary PCI (hours)	3.40 (2.23)	3.96 (2.26)
Statin use within 7 days of randomization no.(%)	8 (21.05)	8 (26.67)
Statin use after randomization		
Atorvastatin 40-80 mg or Rosuvastatin 40 mg daily	37 (97.37)	30 (100)
Atorvastatin 80 mg or Rosuvastatin 40 mg daily	37(97.37)	27(90.00)
Ezetimibe	2 (5.26)	1 (3.33)

Primary Outcome

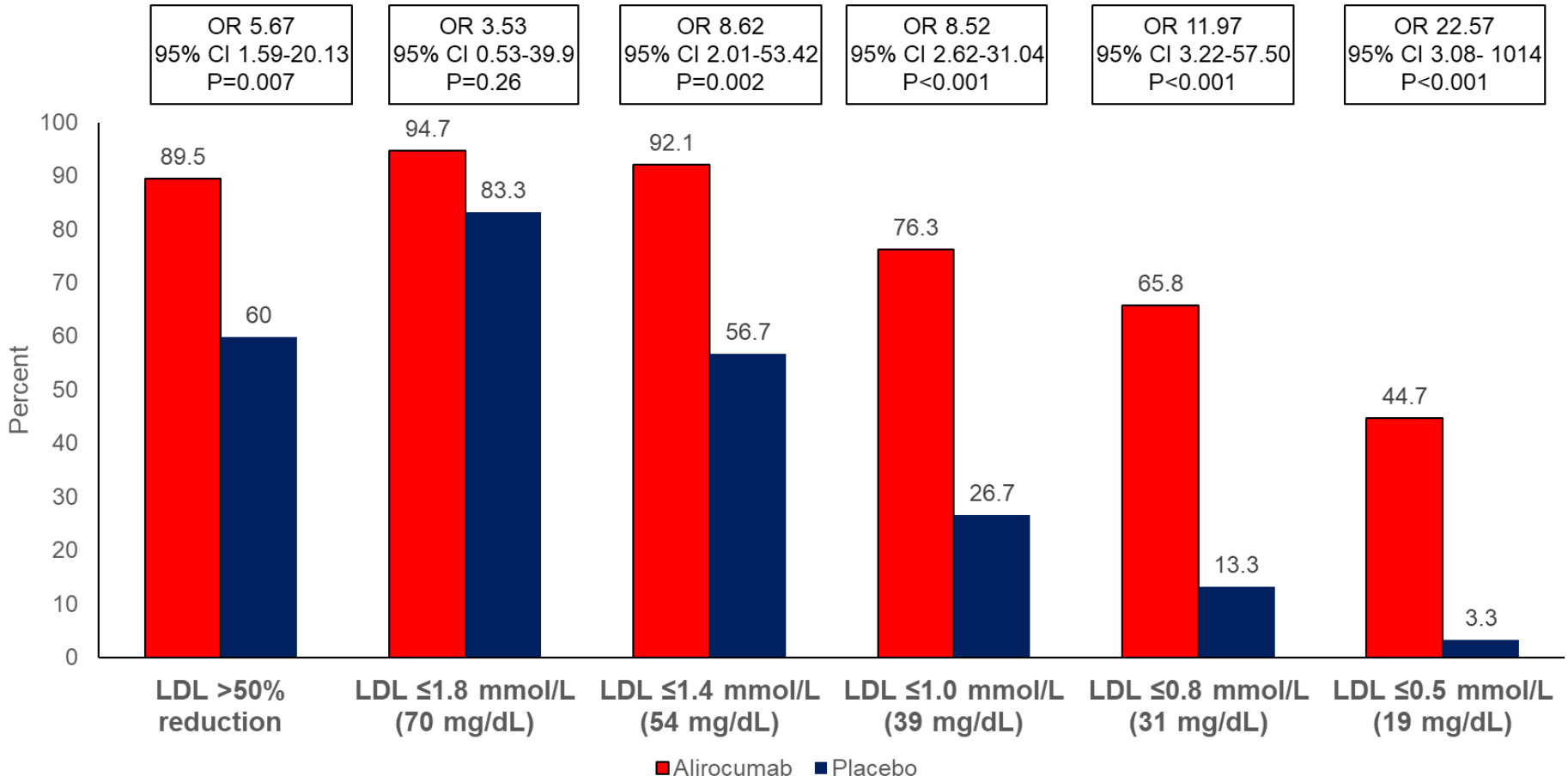
LDL Reduction at 6 weeks (median 42 days)



Timing of LDL reduction



LDL Targets


OR 5.67
95% CI 1.59-20.13
P=0.007
OR 3.53
95% CI 0.53-39.9
P=0.26
OR 8.62
95% CI 2.01-53.42
P=0.002
OR 8.52
95% CI 2.62-31.04
P<0.001
OR 11.97
95% CI 3.22-57.50
P<0.001
OR 22.57
95% CI 3.08- 1014
P<0.001
Percent
100
90
80
70
60
50
40
30
20
10
0
89.5
60
94.7
83.3
92.1
56.7
76.3
26.7
65.8
13.3
44.7
3.3
LDL >50% reduction
LDL ≤1.8 mmol/L (70 mg/dL)
LDL ≤1.4 mmol/L (54 mg/dL)
LDL ≤1.0 mmol/L (39 mg/dL)
LDL ≤0.8 mmol/L (31 mg/dL)
LDL ≤0.5 mmol/L (19 mg/dL)
Alirocumab
Placebo

Conclusions

In patients with STEMI undergoing primary PCI, the routine early initiation of PCSK9 inhibitor *(regardless of baseline LDL level or prior statin use)* compared with sham-control:

1. Reduced LDL-cholesterol by 22% at 6 weeks (median 45 days) on a background of high intensity statin therapy.
2. Resulted in a greater proportion of patients achieving >50% reduction or ESC LDL target of ≤ 1.4 mmol/L (70 mg/dL).
3. Appeared to be feasible and safe.

Implications

- Routine, early administration of PCSK9 inhibitor has the potential to *substantially reduce morbidity and mortality globally* after high-risk ACS by further reducing LDL beyond statins in a *much* greater number of high-risk patients than is currently treated with these agents.
- A large outcomes trial evaluating this simplified strategy is needed

EPIC STEMI

Simultaneous Publication
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EuroIntervention

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