Effect of Alirocumab in Patients With or Without Prior Revascularization and Recent Acute Coronary Syndrome in the ODYSSEY OUTCOMES Trial

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Background

- The ODYSSEY OUTCOMES trial compared the PCSK9 inhibitor alirocumab with placebo in 18,924 patients (pts) with a recent acute coronary syndrome (ACS).[1]
- Alirocumab reduced the incidence of the primary outcome of major adverse CV events (MACE): death from coronary heart disease, non-fatal myocardial infarction, ischemic stroke, or hospitalization for unstable angina. Alirocumab was also associated with fewer deaths and ischemia-driven coronary revascularization (REVASC).

Aim

- To determine the effect of alirocumab on MACE and death according to prior REVASC, and first and total coronary REVASC procedures (prespecified analysis).

Methods

- Coronary REVASC included coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI). Pts were categorized at baseline by whether they had prior REVASC (before the qualifying ACS) or index revascularization (for the qualifying ACS). Pts with prior and index REVASC were included in the index category.
- Pts were randomized to treatment with alirocumab or placebo 1–12 months after ACS, after completion of all planned coronary REVASC.
- Ischemia-driven coronary REVASC was defined as REVASC performed after randomization for new or progressive anginal symptoms; new or progressive abnormalities on stress testing; and recurrent acute ischemia (i.e. ACS). It excluded procedures performed solely for restenosis at a prior PCI site.
- Treatment effects on first and total events were summarized by hazard ratios (HR) from proportional hazard models and mean cumulative function rates, with death as a competing event.

Table 1. Baseline characteristics by prior revascularization status

	No revascularization (n=4045)		Index (± prior) revascularization (n=13677)		Prior revascularization only (n=1202)	
	ALI (n=2072)	PBO (n=1973)	ALI (n=6799)	PBO (n=6878)	ALI (n=591)	PBO (n=611)
Age, years	59 (52, 66)	59 (52, 66)	58 (51, 64)	58 (52, 65)	61 (54, 67)	60 (53, 67)
Women	672 (32.4)	615 (31.2)	1572 (23.1)	1628 (23.7)	146 (24.7)	129 (21.1)
White	1542 (74.4)	1459 (73.9)	5454 (80.2)	5544 (80.6)	504 (85.3)	521 (85.3)
NSTEMI (index event)	1136 (54.8)	1086 (55.0)	3052 (44.9)	3126 (45.4)	386 (65.3)	389 (63.7)
High-dose statin	1860 (89.8)	1780 (90.2)	6011 (88.4)	6121 (89.0)	509 (86.1)	530 (86.7)
LDL-C, mg/dL	86 (71, 106)	88 (73, 106)	86 (73, 103)	86 (73, 103)	94 (79, 116)	90 (77, 110)
HDL-C, mg/dL	43 (37, 51)	42 (36, 51)	42 (36, 50)	42 (36, 50)	43 (36, 51)	42 (36, 49)
Lp(a), mg/dL	20 (6, 51)	20 (6, 53)	21 (7, 58)	21 (7, 59)	23 (8, 68)	23 (7, 66)
eGFR <60 mL/min per 1.73 m^2	307 (14.8)	287 (14.5)	837 (12.3)	868 (12.6)	134 (22.7)	106 (17.3)
Diabetes*	658 (31.8)	591 (30.0)	1809 (26.6)	1930 (28.1)	226 (38.2)	230 (37.6)
Hypertension*	1393 (67.2)	1280 (64.9)	4310 (63.4)	4261 (62.0)	502 (84.9)	503 (82.3)
MI*	206 (9.9)	243 (12.3)	1160 (17.1)	1150 (16.7)	428 (72.4)	452 (74.0)
Stroke*	66 (3.2)	62 (3.1)	207 (3.0)	212 (3.1)	33 (5.6)	31 (5.1)
CABG*	0	0	304 (4.5)	322 (4.7)	217 (36.7)	204 (33.4)
PCI*	0	0	1135 (16.7)	1119 (16.3)	491 (83.1)	496 (81.2)
PAD*	58 (2.8)	55 (2.8)	263 (3.9)	278 (4.0)	52 (8.8)	53 (8.7)
Heart failure*	429 (20.7)	390 (19.8)	786 (11.6)	896 (13.0)	151 (25.5)	163 (26.7)
Aspirin	1924 (92.9)	1829 (92.7)	6564 (96.5)	6630 (96.4)	562 (95.1)	577 (94.4)
$P2Y_{12}$ antagonist	1665 (80.4)	1559 (79.0)	6161 (90.6)	6207 (90.2)	470 (79.5)	479 (78.4)
ACE-I/ARB	1577 (76.1)	1518 (76.9)	5304 (78.0)	5349 (77.8)	475 (80.4)	493 (80.7)
Beta-blocker	390 (18.8)	388 (19.7)	977 (14.4)	996 (14.5)	94 (15.9)	84 (13.7)

*Medical history before index event. ACE-I, angiotensin-converting enzyme inhibitor; ALI, alirocumab; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; Lp(a) lipoprotein(a); MI, myocardial infarction; NSTEMI, non-ST-segment elevation MI; PAD, peripheral artery disease; PBO, placebo; PCI, percutaneous coronary intervention.

Figure 1. Rate and effect on first and total coronary revascularizations by revascularization status and treatment allocation

*Four years after randomization. HRs reflect stratification by geographic region. CI, confidence interval.

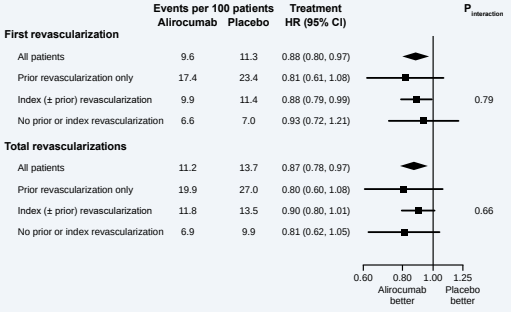
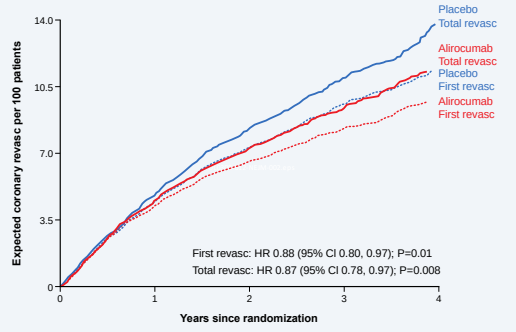


Figure 2. Cumulative incidence of first and total coronary revascularizations by treatment allocation



Results

- Of 13,677 (72.3%) pts who had index REVASC (66.9% PCI only, 4.8% CABG only, 0.6% both), 2533 (13.4%) also had undergone prior REVASC. There were 1202 (6.4%) pts who had prior but not index REVASC and 4045 (21.4%) had neither prior nor index REVASC.
- Baseline characteristics by REVASC category are shown in Table 1. Pts with prior REVASC had a greater burden of comorbidities and risk factors.
- Alirocumab reduced first and total coronary REVASC without heterogeneity according to prior or index REVASC status (Figure 1). However, absolute reduction in REVASC with alirocumab was greatest in pts with prior REVASC.
- The effect of alirocumab on cumulative first and total coronary REVASC was minimal during the first year after randomization and greater thereafter (Figure 2).

Conclusions

- **Alirocumab significantly reduced first and total ischemia-driven coronary revascularizations in patients with recent ACS, independent of prior or index revascularization.**
- **The treatment effect of alirocumab on MACE and all-cause death was consistent regardless of prior revascularization.**

Reference

Schwartz G, et al. NEJM 2018;379:2097–107.

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