Evolocumab and complex coronary revascularization during 8-year follow-up: Analysis from the FOURIER and FOURIER OLE trials

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on behalf of the FOURIER and FOURIER OLE investigators

An Academic Research Organization of
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Background

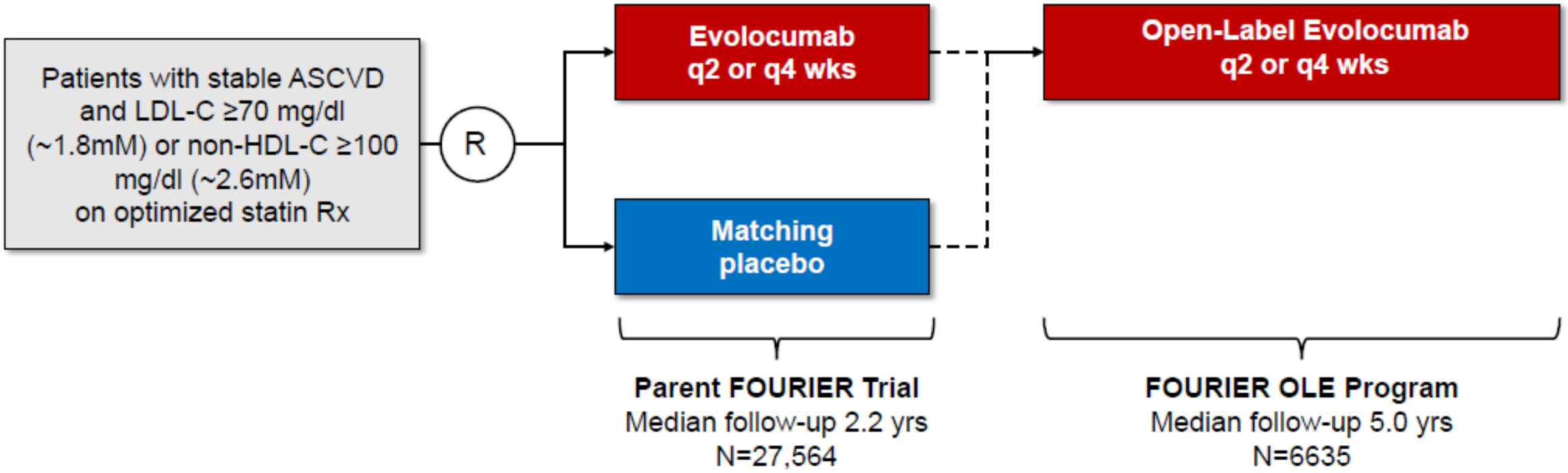
- **The extent of coronary plaque burden is associated with long-term outcomes and impacts clinical decision-making[1]**
  - Higher plaque burden ➔ more complex CAD ➔ worse prognosis
  - Complex CAD may require complex revascularization (complex PCI or CABG)

- **In FOURIER, the PCSK9i evolocumab reduced the incidence of MACE and complex coronary revascularization in patients with ASCVD[2,3]**

- **The FOURIER Open Label Extension (OLE) allows for longer-term follow-up and assessment of early vs later initiation of evolocumab[4]**

[1]Wykrzykowska JJ et al JACC 2010 | [2]Sabatine et al. NEJM 2017 | [3]Oyama et al. JACC 2021 | [4]O'Donoghue et al. Circulation 2022

Study Schema: FOURIER and OLE



Objective

To investigate the effect of early vs. delayed initiation of evolocumab on complex coronary revascularization

Methods

- **FOURIER and FOURIER-OLE**
  - FOURIER: 27,564 patients with median 2.2 years follow-up
  - FOURIER OLE: 6,635 patients with additional median 5.0 years follow-up, max. (8 years)
  - Analysis of all patients unless indicated otherwise

- **Primary outcome: complex coronary revascularization[1]**
  - Complex PCI (GLOBAL LEADERS definition)
    - One of the following: multivessel PCI, ≥3 stents implanted, ≥3 lesions treated, bifurcation PCI with ≥2 stents, or total stent length >60 mm.
  - CABG

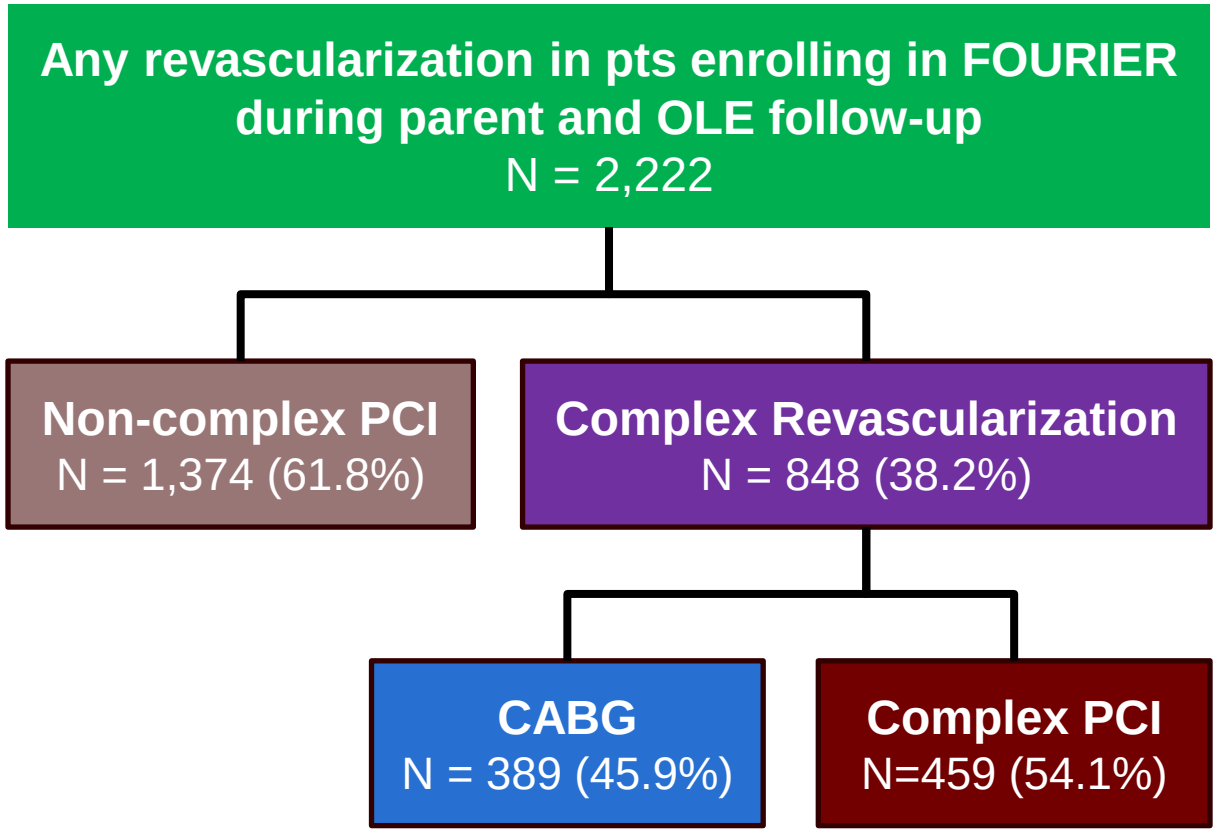
- **Central assessment of the primary outcome using data provided by the local investigators to the Clinical Event Committee blinded to randomized group**

[1]Oyama et al. JACC 2021

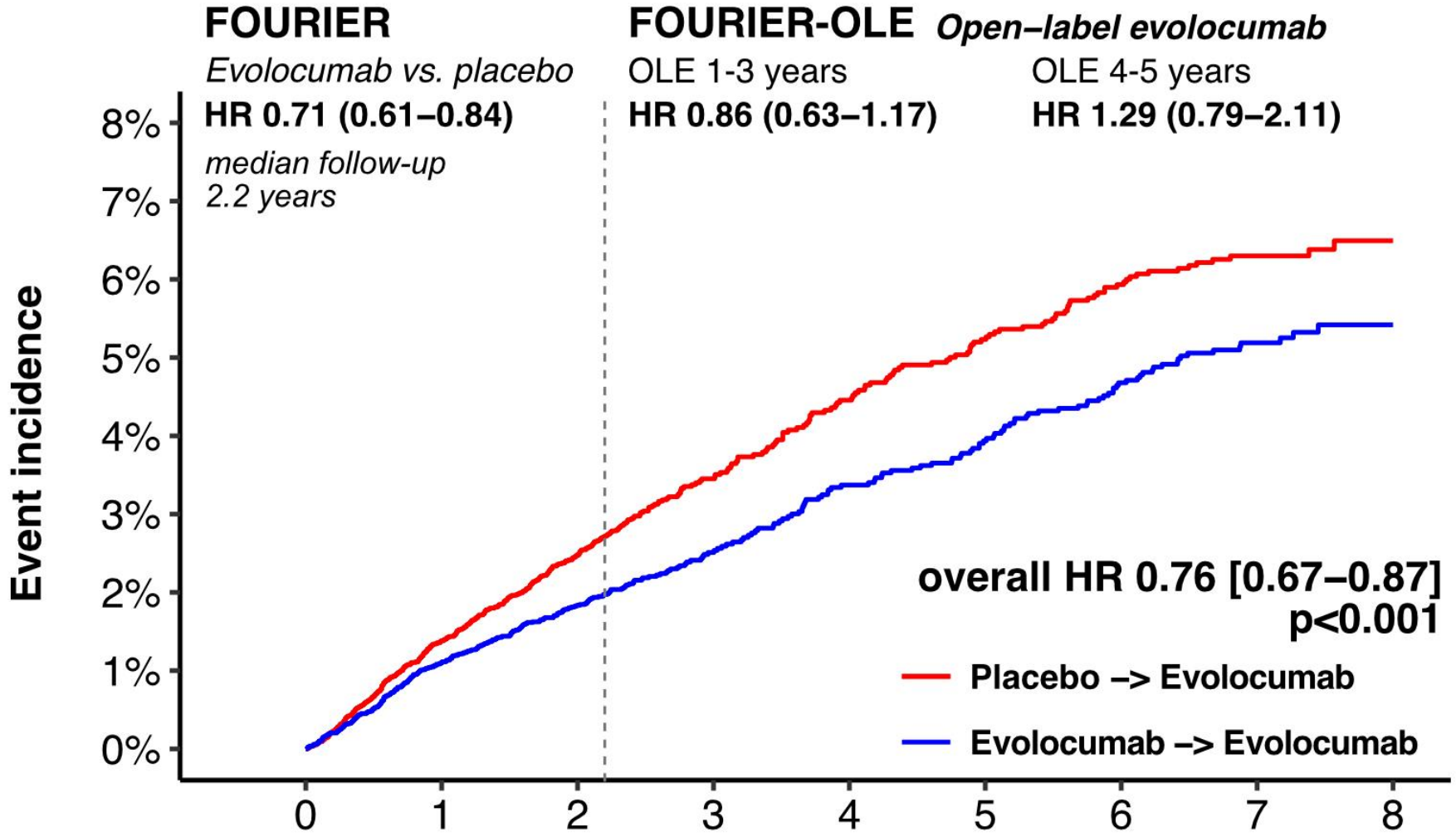
Baseline characteristics & revasc events

	FOURIER	OLE
Age	63 (9)	62 (9)
Female	25	23
Hypertension	80	83
Diabetes	37	34
Smoking	28	27
Prior myocardial infarction	81	84
Non-hem. stroke	19	16
Peripheral artery disease	13	14
Prior coronary revascularization	66	74
High-intensity statin use	69	77
Ezetimibe	5	6

mean (SD) or %

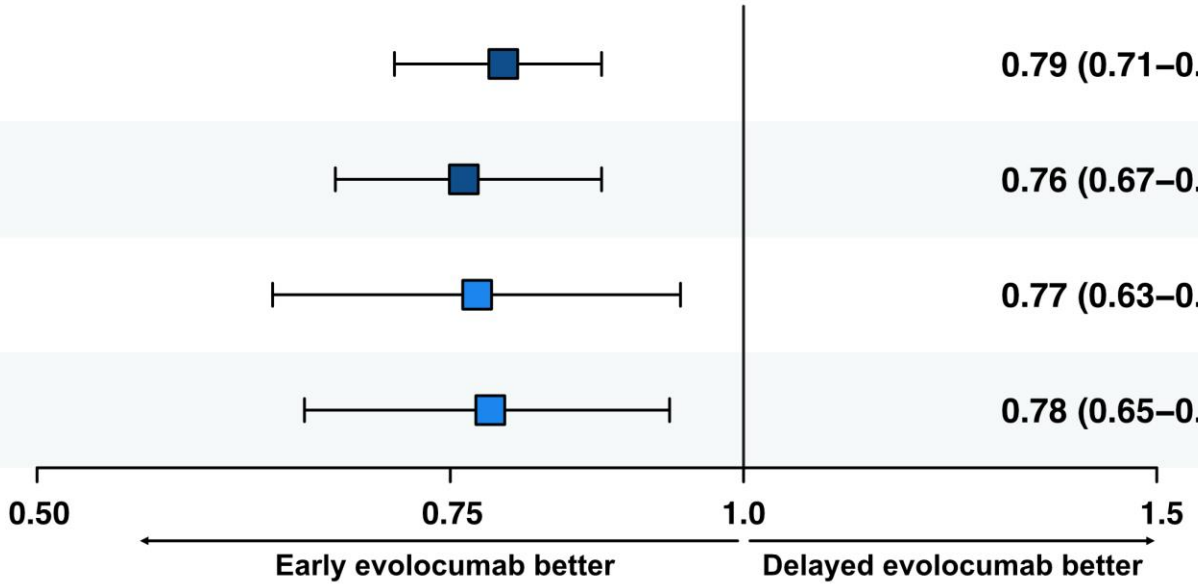


Complex coronary revasc – FOURIER & OLE

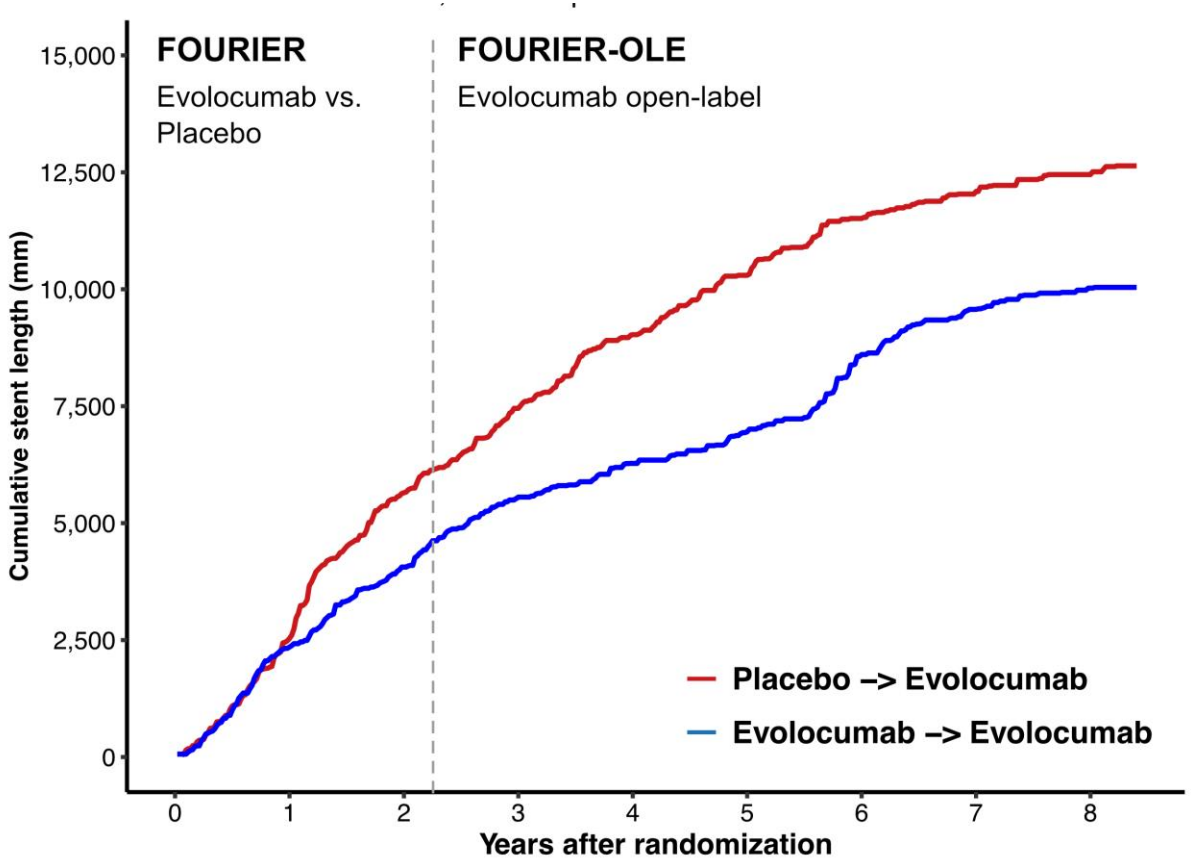


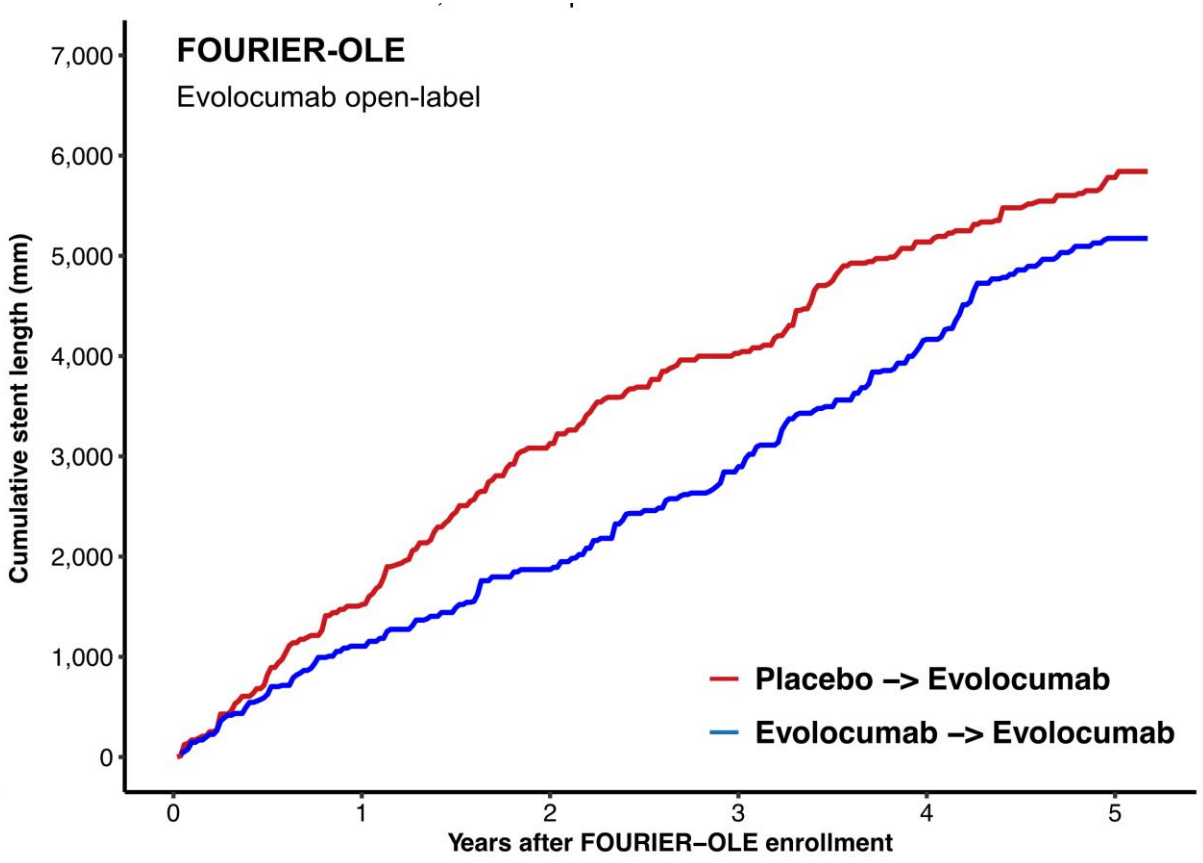
Endpoints components

	Event count Initial Randomization Placebo	Evolocumab	HR (95% CI)	P–Value
Non–complex PCI	872	697	0.79 (0.71–0.87)	<0.001
Complex revascularization (CABG or complex PCI)	478	370	0.76 (0.67–0.87)	<0.001
CABG	219	170	0.77 (0.63–0.94)	0.01
Complex PCI	268	211	0.78 (0.65–0.93)	0.006



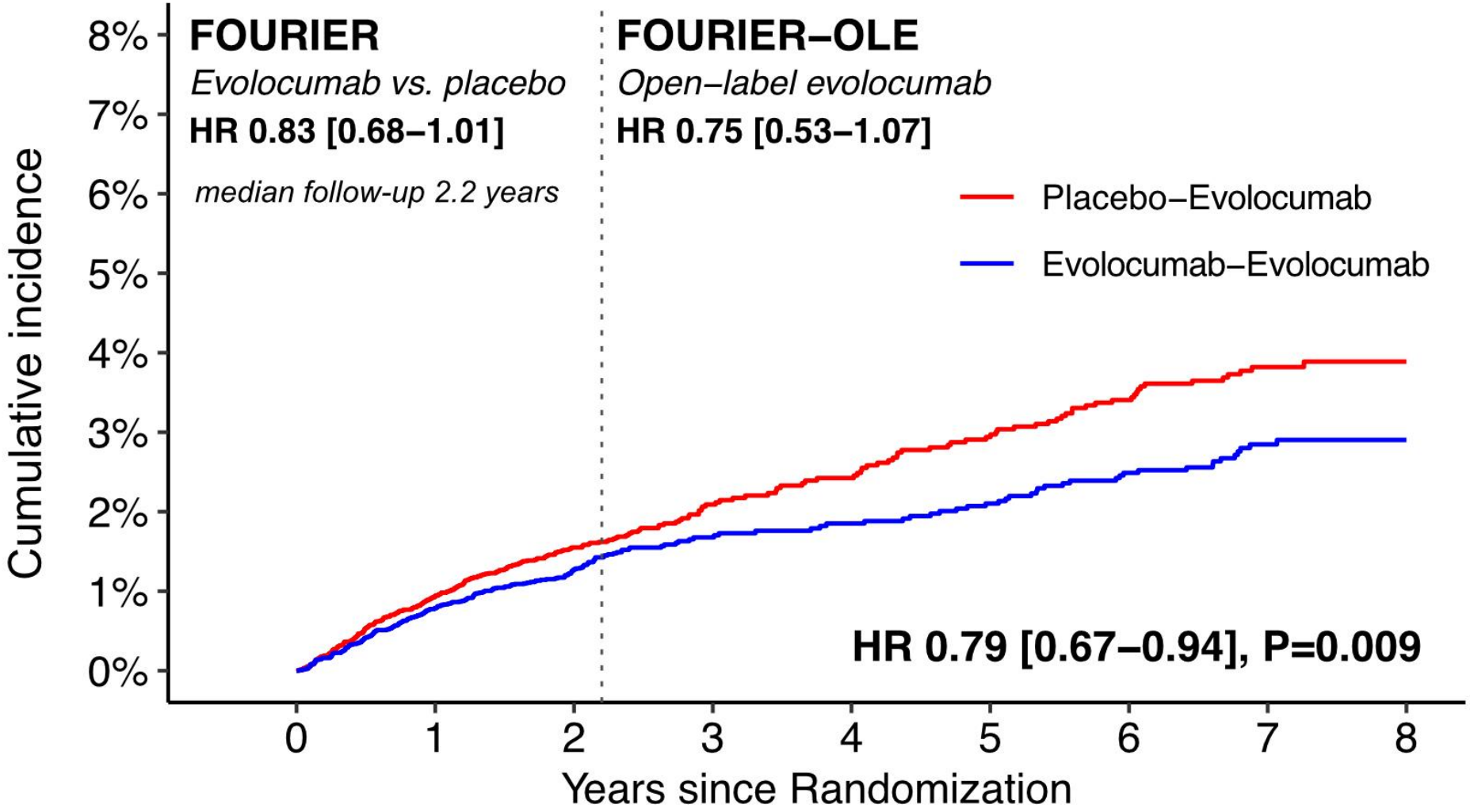
Cumulative coronary stent length





Analysis restricted to patients enrolled in OLE

Revascularization for in-stent-restenosis



Limitations

- **Extended follow-up was available for ~24% of patients.**
  - FOURIER ~60,000 patient-years | in OLE additional ~33,000 patient-years.

- **Details on coronary anatomy were only available for patients undergoing coronary revascularization.**

- **The outcome was defined post-hoc with central assessment of complex revascularization using data provided by local investigators.**

Conclusion

- **Early versus delayed therapy with evolocumab reduces the incidence of complex coronary revascularization during long-term follow-up.**
  - This includes complex PCI as well as CABG and is reflected by less stent material implanted and a lower rate of revascularization for in-stent-restenosis.

- **These findings highlight the benefits of early initiation of potent LDL-C reduction in patients with established ASCVD.**

Thank you very much for your attention!