Impact of Lowering LDL-C with Evolocumab on Patient-Reported Cognition in Participants from the FOURIER Trial

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BACKGROUND

- In the FOURIER trial, evolocumab did not increase neurocognitive, even in patients with very low LDL-C (<20 mg/dL).
- In the EBBINGHAUS trial, evolocumab did not affect cognitive function among 1204 patients who underwent computed-based cognitive testing.
- To date, patient-reported cognition outcomes have not yet been described in a large trial of PCSK9 inhibitors.

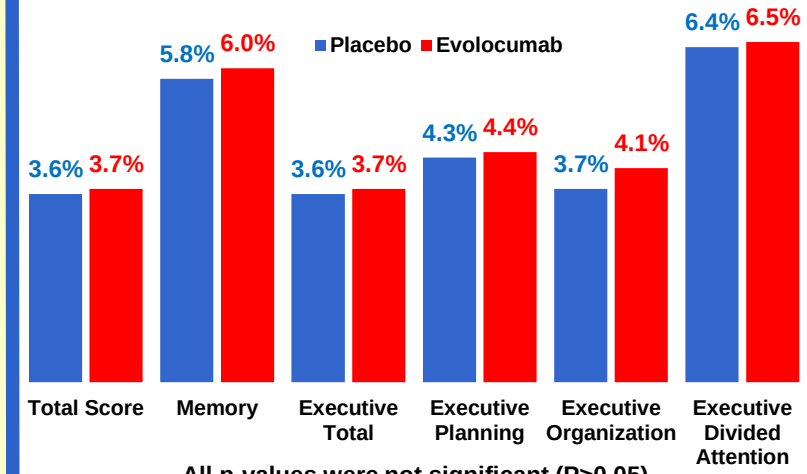
METHODS

- In FOURIER, 27564 patients with ASCVD were randomized to evolocumab vs. placebo on top of maximal statin for a median FUP of 2.2 years.
- 22655 patients completed the Everyday Cognition (ECog) questionnaire (23 items for memory and executive functions) at the end of the trial.
- Changes in each item were rated on a four-point scale:
  1-Better or No change.
  2-Questionnable or occasionnally worse.
  3-Consistently a little worse.
  4-Consistenty much worse.
- Decline in patient-reported cognition (average ECog ≥2 vs. <2) was reported for each domain by treatment arm at the end of the trial.
- Decline in patient-reported cognition at the end of the trial was reported by achieved on-treatment LDL-C levels at 4 weeks were reported adjusting for age, sex, race, BMI, region of enrollment, P2Y12 inhibitors and baseline LDL-C.

1.Baseline Characteristics

Characteristics	Placebo, N=11292	Evolocumab N=11363
Mean Age	63	63
Age ≥ 75 years, %	9	9
Male, %	76	76
White race, %	85	85
Nonhemorrhagic stroke, %	19	19
Neurological disorder, %	9	9
Atrial fibrillation, %	8	8
Hypertension, %	79	79
Diabetes, %	36	36
Median LDL-C (mg/dL)	91.5	91
High intensity statin, %	68	69

2. Decline in patient-reported cognition (ECog ≥2) at the end by baseline randomized treatment arm

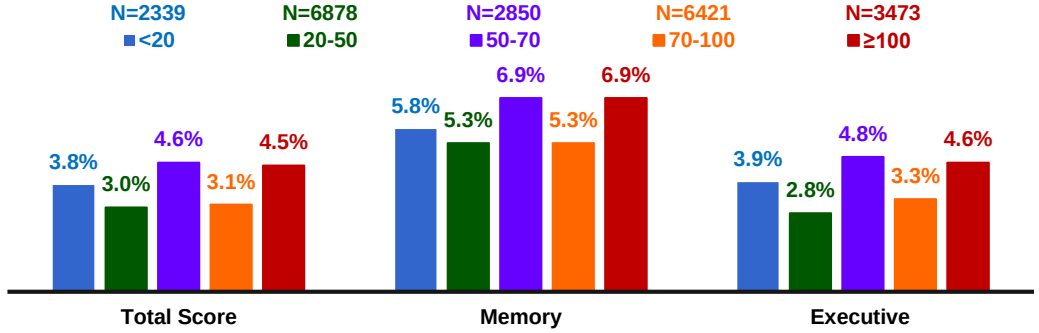


All p-values were not significant (P>0.05)

3. Decline in patient-reported cognition (total Ecog score ≥2) at the end by baseline univariate subgroups

Univariate Subgroup	Placebo	Evolocumab	P-int
Age < 75 years , %	3.2	3.4	0.14
Age ≥ 75 years, %	7.4	6.1	
Male, %	3.2	3.2	0.41
Female, %	4.7	5.3	
Baseline LDL-C ≥ 85mg/dL, %	3.7	3.8	0.91
Baseline LDL-C < 85 mg/dL, %	3.3	3.4	
Prior Cerebrovascular disease, %	5.3	5.5	0.99
No Cerebrovascular disease, %	3.0	3.2	

4. Decline in patient-reported cognition (ECog ≥2) at the end by achieved LDL-C (mg/dL) at 4 weeks



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SUMMARY

- The change in patient-reported cognition from the start to the end of the trial was similar for evolocumab and placebo in the overall population and in major subgroups.
- There were no differences in cognition in patients grouped by achieved LDL-C even for those with LDL-C <20 mg/dL at 4 weeks.

CONCLUSION

Treatment with evolocumab in addition to maximally tolerated statin therapy did not affect patient-reported cognition after an average of 2.2 years of treatment.

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