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

Baris Gencer,¹ François Mach,² Jianping Guo,¹ Kyungah Im,¹ Andrea Ruzza,³ Huei Wang,³ Christopher E. Kurtz,³ Terje R. Pedersen,⁴ Anthony C. Keech,⁵ Brian R. Ott,⁶ Marc S. Sabatine,¹ Robert P. Giugliano¹

¹TIMI Study Group, Division of Cardiovascular Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; ²Cardiology Division, Geneva University Hospitals, Switzerland; ³Amgen, Thousand Oaks, CA; ⁴Ullevaal and Medical Faculty, University of Oslo, Norway; ⁵National Health and Medical Research Council Clinical Trials Center, University of Sydney, Australia; ⁶Alzheimer’s disease and Memory Disorders Center, Rhode Island Hospital, Brown University, Providence, RI

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. Questionable or occasionally worse.
  3. Consistently a little worse.
  4. Consistently 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.

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.