Introduction:
• There was inconclusive evidence on neurocognitive side effects of PCSK9 inhibitors from early clinical trials with lack of proper methodology to assess cognitive function.
• A recent study that prospectively evaluated cognitive function in patients who received PCSK9 inhibitor therapy or placebo using the Cambridge Neuropsychological Test Automated Battery found no significant between-group difference. [1]

Objective:
• To evaluate cognitive function in patients receiving evolocumab at Mayo Clinic using a personalized validated neuropsychological tool that assesses multiple domains administered by a single experienced psychologist.

Methods:
• Patient population: a subgroup of patients who were started on evolocumab between Jan 2015 to Dec 2017 at Mayo Clinic in Rochester MN.
• Prospectively assessed cognitive function using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) at baseline prior to therapy initiation and 10-20 months after starting therapy.
• RBANS consists of 10 subtests which give 5 scores for the 5 domains tested:
  1) Immediate memory
  2) Visuospatial/constructional
  3) Language
  4) Attention
  5) Delayed memory
• Analysis:
  • Paired t-test
  • p <0.05 is considered statistically significant.

Results:
• Nine patients who received evolocumab underwent neuropsychological assessment with RBANS before and 10-20 months after initiation of therapy.
• Patient characteristics (n =9):
  • Mean age: 59 yrs ±9
  • Male: 4/9
  • Average education: 15 yrs ±2.6
  • BMI: 28 ±4
  • Familial hypercholesterolemia: 8/9
  • Coronary artery disease: 7/9
  • Hypertension: 6/9
  • Diabetes: 0/9
  • Stroke/TIA: 1/9
  • Tobacco: 3/9 former smokers

Table 1:
The 5 RBANS domains and the total score in 9 patients on evolocumab pre- and post-treatment.

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<tr>
<th>INDEX/DOMAIN</th>
<th>Mean difference (SD)</th>
<th>p value</th>
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<tr>
<td>Immediate memory</td>
<td>-1.78 (13.26)</td>
<td>0.70</td>
</tr>
<tr>
<td>Visuospatial/constructional</td>
<td>6.56 (13.79)</td>
<td>0.19</td>
</tr>
<tr>
<td>Language</td>
<td>-4.11 (12.58)</td>
<td>0.36</td>
</tr>
<tr>
<td>Attention</td>
<td>-1.07 (7.37)</td>
<td>0.51</td>
</tr>
<tr>
<td>Delayed memory</td>
<td>2.67 (8.31)</td>
<td>0.36</td>
</tr>
<tr>
<td>Total scale</td>
<td>0.44 (6.11)</td>
<td>0.83</td>
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Conclusions
There was no significant change in cognitive function in multiple domains observed in patients receiving evolocumab over an average of 15 months.

References:
Table 1
The 5 RBANS domains and the total score in 9 patients on evolocumab pre- and post- treatment.

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Figure 1
Mechanism of action of PCKS9 inhibitors [2].

Hypercholesterolemia and monoclonal antibodies to PCSK9
Proprotein convertase subtilisin/kexin type 9 serine protease (PCSK9) plays an important role in cholesterol metabolism by regulating LDL receptor degradation. Binding of circulating PCSK9 by parenteral monoclonal antibodies results in augmented recirculation of the LDL receptor to the hepatocyte surface and accelerated clearance of circulating LDL-C.