Evolocumab use in Europe: clinical guidelines vs. reimbursement thresholds – results from the HEYMANS study

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Background: 2019 ESC/EAS guidelines recommend a 50% lowering in untreated LDL-C and use of PCSK9 inhibitors (PCSK9i) for patients (pts) at very high cardiovascular (CV) risk when LDL-C goals of <1.4mmol/L are not met despite maximally tolerated statins and ezetimibe. However, the LDL-C threshold at which PCSK9i are reimbursed are higher than the goals recommended in clinical guidelines.

Purpose: This prospective observational cohort study describes clinical characteristics and LDL-C control among pts initiating evolocumab across 12 EU countries.

Methods: Pts are followed from evolocumab initiation (baseline). Demographic/clinical characteristics, lipid lowering therapy (LLT) and lipid values are being collected from medical records (6 months before evolocumab up to 30 months post initiation). We report interim data from pts initiating evolocumab from August 2015 followed-up until July 2020.

Results: Of the 1,952 pts in whom evolocumab was initiated as per local reimbursement criteria, most (1844 [94%]) had 12 months follow-up, 785 (40%) had 24 months follow-up; mean follow-up: 20 months. Mean (SD) age was 60 (10.8) years; 85% of pts had a history of CV disease, 45% had familial hypercholesterolemia, 19% had type 2 diabetes, 65% were hypertensive, 7% had chronic kidney disease and 51% were prior/current smokers. At evolocumab initiation, 60% reported statin intolerance and 41% were on no background LLT. Fewer than half (846 [43%]) were receiving a statin (± ezetimibe); of these, most received a high/moderate intensity (68%/22%), with 13% receiving statin monotherapy. Median (Q1, Q3) baseline LDL-C was 3.98 (3.17, 5.07) mmol/L. Within 3 months of initiation median LDL-C fell by 58% to 1.63mmol/L. This reduction was maintained over time (Figure 1). Overall, 58% of pts achieved at least one LDL-C <1.4mmol/L during follow-up. Among pts receiving background statins ± ezetimibe at evolocumab initiation, 67% (710/1053) achieved at least one LDL-C <1.4mmol/L, versus 44% (317/714) of pts not receiving background statins/ezetimibe. During follow-up background oral LLT did not materially change; 40–45% pts received no LLT, 41–44% received statin ± ezetimibe, 12–14% received statin monotherapy.

Conclusion: In Europe, pts initiated on evolocumab had baseline LDL-C levels almost 3x higher than the present threshold for PCSK9i use recommended in guidelines reflecting disparities between local reimbursement criteria and guidelines. Although evolocumab led to a >50% reduction in LDL-C, only ~50% pts achieved an LDL-C <1.4mmol/L, as approximately 41% received only evolocumab as monotherapy. LDL-C goal attainment was however higher among pts receiving evolocumab with background LLT. Therefore, lowering the LDL-C threshold for PCSK9i reimbursement, would result in more patients receiving combination therapy with oral LLT plus PCSK9i, thus increasing the likelihood of more pts achieving very-high risk LDL-C goals.

Figure 1 - LDL-C levels and percent change after evolocumab initiation