First clinical experiences with inclisiran in real world setting

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Background: Inclisiran is the first-in-class small interfering RNA (siRNA) PCSK9 inhibitor. In clinical trials, inclisiran showed effective and sustained LDL-C reduction of approximately 50%. However, data about the efficacy and safety in clinical setting are scarce. We aim to investigate the efficacy and safety in clinical practice.

Methods: Registry of all consecutive patients who started with inclisiran at a lipid clinic of a university hospital. Patients were eligible if they fulfilled reimbursement criteria in the Netherlands; very high risk patients with FH and/or ASCVD and not on target LDL-C levels despite maximally tolerated oral lipid lowering medication. Patients were included if they started with inclisiran as first line (group 1) or switched from PCSK9 monoclonal antibody (mAbs) to inclisiran (group 2). LDL-C levels were measured 3 months after administration of inclisiran initiation. Median change of LDL-C levels was calculated on an individual and group level.

Results: We analysed 50 patients (26 women, 33 patients with FH), median [25th percentile; 75th percentile] age of 64 [52; 68] years. Patients who newly started Inclisiran (group 1) showed a LDL-C decrease of 39 [-50; -33]%. Patients who used statins as co-medication had a higher median LDL-C decrease compared to those without statin use (45% vs. 38%). However, patients who switched from mAbs to Inclisiran (group 2) had an increase in LDL-C of +41 [+3; +97]% (figure 1).

Almost half of the patients (42%) experienced a mild burning sensation. During follow-up 6 patients (12%) reported side effects as abdominal complains, dizziness, fatigue and flu-like symptoms in the first week after administration. One patient stopped treatment because of perceived side effects like fatigue and myalgia.

Conclusions: Our initial experience of inclisiran in a clinical setting showed slightly less reduction in LDL-C levels compared to clinical trials but a similar safety profile. Moreover, patients who switched from PCSK9 mAbs to inclisiran showed an increase in LDL-C levels implying that inclisiran is less potent in LDL-C reduction compared to PCSK9 mAbs.

Figure 1 LDL-C change of individual patients (n=50) 3 months after initiation of inclisiran