

## CHARACTERIZATION OF NEW USERS OF PCSK9INHIBITORS IN TUSCANY: A DRUG UTILIZATION STUDY BASED ON REGIONAL ADMINISTRATIVE DATA

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**Background and aim:** Cardiovascular (CV) ischemic disease represents a major cause of death and severe medical condition worldwide. The high circulating level of low-density lipoprotein cholesterol (LDL-C) is considered a cause of CV ischemic diseases. Different Lipid Lowering Therapies (LLTs) have been authorized to reduce LDL-C level to prevent CV events, both in primary and secondary prevention. In the last years two new LLTs (i.e. evolocumab and alirocumab), called Proprotein Convertase Subtilisin/Kexin type nine inhibitors (PCSK9is), have been approved. The National Healthcare Service (NHS) granted the reimbursement of these drugs under specific patient eligibility criteria established by AIFA, also due to their high costs. The aims of this study were to characterise patients starting a PCSK9i therapy in Tuscany during the first reimbursement year and to describe their pattern of use.

**Methods:** All residents in Tuscany region, accounting for approximately 3.7million of inhabitants, were included in the study. Individuals receiving at least one dispensation of evolocumab (ATC code: C10AX13) or alirocumab (C10AX14) from July 2017to June 2018were selected. Characteristics of these patients were retrieved into all available healthcare administrative databases: inhabitant registry, registry of exemptions from co-payment, outpatient drug dispensing- and hospital discharge-database. For each treated individual, socio-demographic characteristics (age, sex, educational level) were described, as well as clinical conditions increasing CV risk (hypercholesterolemia, diabetes, chronic renal failure, chronic hepatitis and pancreatitis). Previous CV events were searched by using hospital discharge database since 1996, in order to distinguish between primary and secondary prevention users. Use of any LLTs therapy in the previous 6months was assessed. The pattern of PCSK9i use in the first 6months of treatment was also analysed in terms of adherence (proportion of days covered PDC  $\geq$  75%), persistence (no gap > 30 days between two dispensations or end of follow-up) and concomitant LLTs.

**Results:** In the observed period, 269patients (7.2per 100,000 inhabitants) started a therapy with PCSK9i: 176used evolocumab and 93alirocumab. Among these, 189(70%) were in secondary prevention. Patients were mostly male (71%), especially among those in secondary prevention (77%). The mean age was 59years old with a "medium" and "lower" educational level (57%). 68% of patients were affected by  $\geq$ 1condition increasing CV risk. For patients in secondary prevention the treatment with PCSK9i started on average 4.8years after the last CV event. In the previous six months, 61% of patients received at least one prescription of high intensity LLTs (i.e. ezetimibe, atorvastatin and rosuvastatin), 16% of low intensity LLTs (other statins, fibrates or omega 3) and 23% did not receive any LLTs. During the follow-up, 80% were adherent to the treatment with no difference between two drugs. 73% were persistent and only 7.5% discontinued the treatment after the first month of treatment. Switching between the two different drugs was observed only in 1case. During the follow-up, 21% of patients received high intensity LLTs concomitantly to the PCSK9i, whereas 10% low intensity LLTs.

**Conclusion:** During the first year since NHS reimbursement approval, the number of PCSK9i users in Tuscany was low. Demographic and clinical characteristics of these patients were in agreement with AIFA eligibility criteria. Patients were mainly in secondary prevention and persistent to previous LLTs, suggesting that they probably did not sufficiently benefit from previous therapies. During the follow-up, patients were adherent and persistent to PCSK9i treatment. Future studies should focus on PCSK9i use during longer time-span to provide evidence on the appropriateness of use, economic impact, and to support regulatory decisions.