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PCSK-9 INHIBITORS FOR THE CONTROL OF HYPERCHOLESTEROLEMIA: ELEGIBILITY FOR TREATMENT, PRESCRIPTION APPROPRIATENESS AND OUTCOMES, IN A REAL-WORLD CLINICAL SETTING

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BACKGROUND AND OBJECTIVES

Several lines of evidence indicate that low-density lipoprotein (LDL) cholesterol increased levels are directly implicated in the development of atherosclerotic cardiovascular (CV) disease with its main clinical manifestations, myocardial infarction and ischemic stroke, currently the leading causes of morbidity and mortality worldwide [1].

The present analysis was conducted to estimate among dyslipidemic patients those potentially eligible for proprotein convertase subtilisin/kexin type 9 inhibitors (iPCSK9), to assess prescription appropriateness and treatment-related outcomes in a real-world clinical practice setting in Italy.

METHODOLOGY

Data source. This retrospective analysis was performed on administrative databases of geographically distributed healthcare entities covering over 3 million health-assisted individuals

Patients' selection. From 2015, this analysis included all the patients with at least one LDL measurement in the 6-months interval before and after the time of the first iPCSK9 prescription (ATC codes: C10AX13, C10AX14).

Study design. The time of the first LDL measurement was the index-date. In the 12 months prior the index-date, the presence of lipid-lowering therapy prescription was investigated.

Adherence to therapy. Patients were defined adherent according to a proportion of days covered (PDC) ≥80%.

Stratification of patients by CV risk profile and lipid target. Patients were stratified by CV risk according to guidelines of the European Atherosclerosis Society and the European Society of Cardiology [2]. For each risk category, a recommended LDL target was defined [2].

VERY HIGH RISK (VHR): diabetes (at least two prescriptions of ATC code A10 or ICD9 250), previous cardiovascular event (ICD-9-CM 410-414, 440, 443), cerebrovascular event (ICD-9-CM 430-438), Chronic Kidney Disease (CKD, ICD-9-CM 585), percutaneous transluminal coronary angioplasty (PTCA, ICD-9-CM V4582, 0066, 3609, 3610). ***TARGET LDL: 55 mg/dL***

HIGH RISK (HR): at least 2 prescriptions of antihypertensives (ATC code C03, C07, C08, C09) or cardiac therapy (ATC code C01) or antiplatelet (ATC code B01AC) or anticoagulants (ATC code B01AA, B01AB). ***TARGET LDL: 70 mg/dL***

OTHER RISK (OR): not included in the previous cohorts. ***TARGET LDL: 116 mg/dL***

Distance-to-target (DTT). For all the patients, DTT was recorded, expressed as difference in mg/dL from current LDL levels and target LDL recommended by guidelines [2].

Eligibility for iPCSK9 treatment. Patients potentially eligible for iPCSK9 treatment were identified in case of failure in reaching the lipid target [2] searched throughout the available period, despite being adherent to previous therapy with high potency statin plus ezetimibe. The achievement of LDL-target was defined considering LDL-index value and thresholds indicated by the guidelines.

REFERENCES

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2. Mach F, et al., Eur Heart J. 2020 Jan 1;41(1):111-188
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RESULTS

PATIENTS POTENTIALLY ELIGIBLE TO iPCSK9 THERAPY

Within the whole sample population of over 3 million individuals, **899,505 patients with at least one LDL determination were included**: 160,811 (17.9%) were under statin treatment, of whom 23,919 (14.9%) under high-potency statins; **1,906 (8.0%) patients received combination of high-potency statins with ezetimibe, and 1,252 (63.9%) resulted adherent to treatment**. Besides, **982 (78.4%) patients failed reaching the LDL-target, thus resulting potentially eligible for iPCSK9 [3]** (**Figure 1A**). Among them, 900 (91.6%) were not treated with iPCSK9 (under-treatment) (**Figure 1B**).

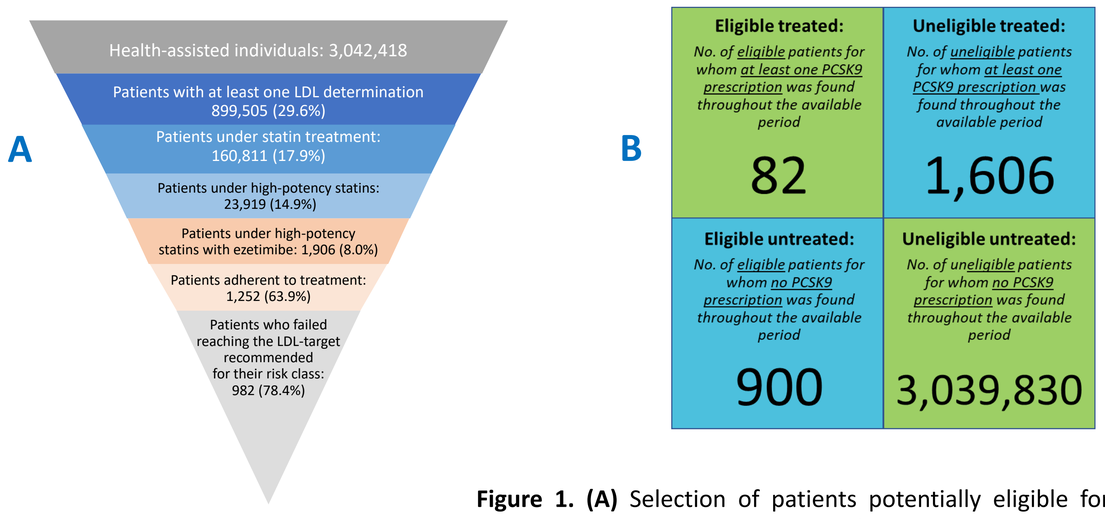

Figure 1. (A) Selection of patients potentially eligible for iPCSK9 therapy. **(B)** Treatment/non-treatment matrix according to eligibility for iPCSK9 therapy.

ACHIEVEMENT OF LIPID TARGET

The **achievement of lipid target was examined in 424 patients** who had at least one available measurement of LDL in the 6 months before and after the start of treatment with iPCSK9 (reported respectively as PRE and POST, in **Figure 2**). The results are presented as DTT in mg/dL (difference in circulating LDL levels from the recommended target) (**Figure 2A**) and as the percentage of non-target subjects (**Figure 2B**) in all 424 patients and in the subgroups divided by CV risk.

The data show reduction in DTT after treatment with iPCSK9 with an overall DTT reduction from 75.4 mg/dL in the 6 months prior to iPCSK9 treatment initiation to 7.2 mg/dL in the following 6 months (**Figure 2A**). On the other hand, a large proportion (93.9%) of the patients did not reach the LDL-target in the 6 months prior to treatment, and this percentage decreased to 47.2% in the 6 months after treatment (**Figure 2B**).

Figure 2. Achievement of lipid target expressed as DTT **(A)** or percentage of patients not-reaching the LDL target **(B).**

CONCLUSIONS

This analysis, **conducted in a setting of real clinical practice in Italy**, allowed to estimate patients potentially eligible for treatment with iPCSK9, to evaluate **their prescribing appropriateness** and the **clinical outcomes** associated with this treatment.

The results showed that a significant proportion of potentially eligible patients are not receiving iPCSK9 therapy, suggesting an undertreatment trend. Furthermore, a reduction in DTT and in the percentage of patients not reaching the lipid target was observed after 6 months of therapy with iPCSK9.

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