Characterization of new users of PCSK9 inhibitors in Tuscany: a drug utilization study based on regional administrative data

Piccinni C[1], Antonazzo IC[2,3], Maggioni AP[1], Pedrini A[1], Calabria S[1], Ronconi G[1], Dondi L[1], Martini N[1], Roberto G[2], Sampietro T[3], Sbrana F[3], Dal Pino B[3], Bigazzi F[3], Lo Surdo G[5], Volpi E[5], Biagini S[5], Gini R[2]

1. Fondazione ReS (Ricerca e Salute) – Research and Health Foundation, Roma, Italy; 2. Epidemiology Unit, Regional Agency for Healthcare Services of Tuscany, Florence, Italy; 3. Pharmacology Unit, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy; 4. Lipoapheresis Unit, reference center for diagnosis and treatment of inherent dyslipidemias – Fondazione Toscana Gabriele Monasterio, Pisa, Italy; 5. Hospital pharmacy, Fondazione Toscana Gabriele Monasterio, Massa, Italy

OBJECTIVE

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.

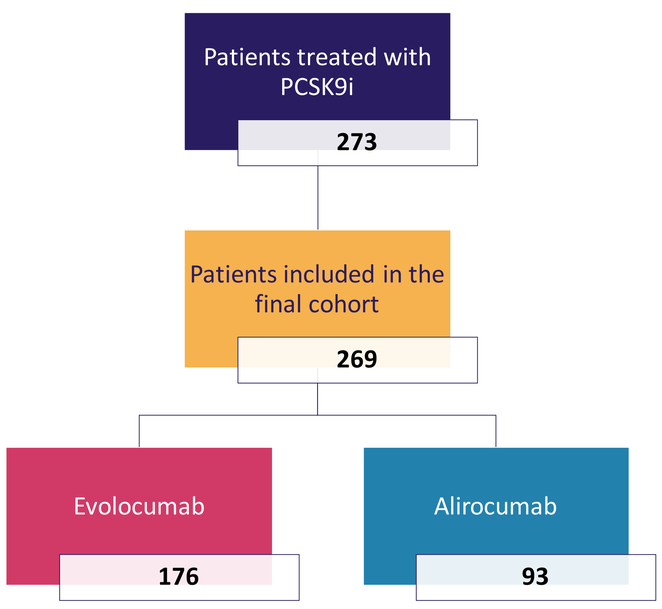
METHODS

Patients on PCSK9-inhibitor administration in Tuscany (3.7 million inhabitants) from 07/2017 to 06/2018 were selected from **regional healthcare administrative databases**. Concomitant use of Lipid-Lowering-Therapies (LLTs), adherence and persistence (no gap ≥60 days between subsequent prescriptions) during the six-months preceding the first PCSK9-inhibitor dispensing, as well as comorbidities since 1996, were described. In the first six-months of PCSK9-inhibitor treatment, adherence (proportion of days covered≥75%), persistence (no gap ≥30 days) were assessed.

RESULTS

New users of PCSK9-inhibitor were 269 (176 evolocumab, 93 alirocumab) (**Fig 1**). The monthly occurrence of PCSK9 inhibitors' new users showed an initial increase (from July 2017 to February 2018), followed by a decrease ending in a plateau in the last observed period (**Fig 2**). We have detected two peaks in November 2017 and in February 2018, corresponding to the end of trials testing evolocumab in Tuscanian patients (i.e. AMG145-20110271; AMG145-20120138; AMG145-20120332 and AMG145-20140316). Patients (mean age of 59.1 years) were mainly male (71.0%) in secondary prevention (70.2%) and affected by familial hypercholesterolemia (53.5%). 66 patients (24.5%) had diabetes and 12 (4.5%) chronic renal failure. **In the six-months preceding the first PCSK9-inhibitor dispensing, 61.3% of patients received at least one prescription of ezetimibe or high intensity statins** and 45.7% were persistent to these drugs (**Tab 1**). During follow-up period (analysed 266 of 269 patients), **80% of patients were adherent to PCSK9-inhibitor and 73% were persistent** (**Tab 2**).

Fig 1 - Selection of new PCSK9i users

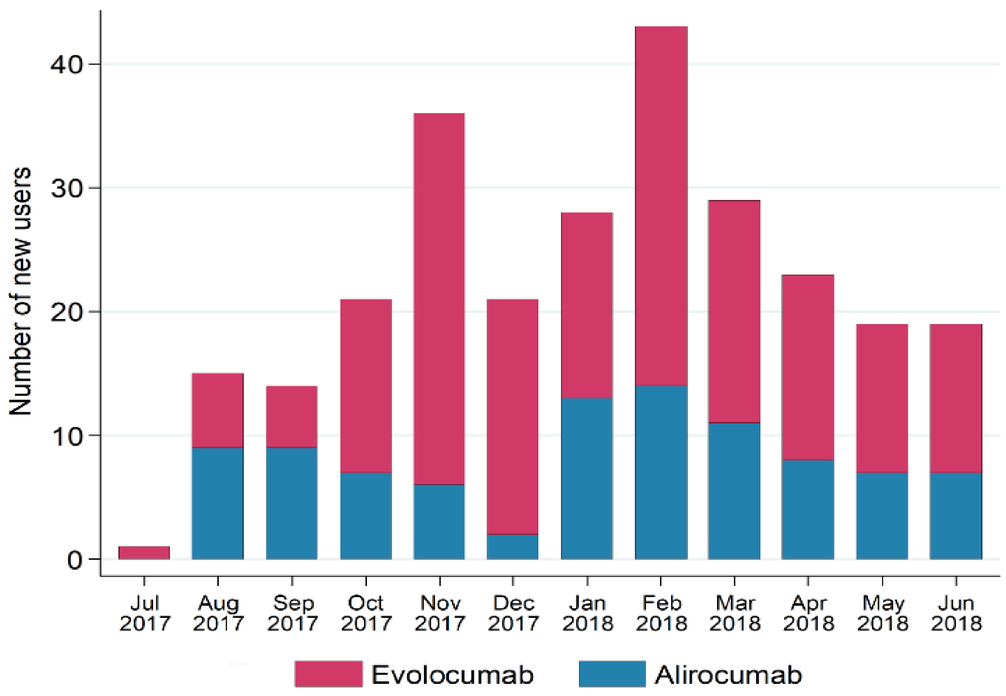


Tab 1 - Lipid lowering therapy in the 6 months previous the PCSK9 inhibitors initiation

PCSK9 inhibitors' new users	Primary prevention N (%) 80 (100)	Secondary prevention N (%) 189 (100)	Total N (%) 269 (100)
Use of LLT during the previous 6 months			
No LLTs	29 (36.3)	31 (16.4)	60 (22.3)
At least one prescription of LLT included in reimbursement criteria*	37 (46.3)	128 (67.7)	165 (61.3)
Only prescription of other LLTs	14 (17.5)	30 (15.9)	44 (16.4)
Persistence to LLT use			
LLT included in reimbursement criteria*	22 (27.5)	101 (53.4)	123 (45.7)
Other LLTs	8 (10.0)	17 (9.0)	25 (9.3)
Patterns of LLT use			
Ezetimibe + moderate/low intensity statin§	13 (16.3)	40 (21.2)	53 (19.7)
Ezetimibe in monotherapy	8 (10.0)	37 (19.6)	45 (16.7)
Ezetimibe + high intensity statins^	9 (11.3)	39 (20.6)	48 (17.8)
High intensity statins^ in monotherapy^	7 (8.8)	12 (6.3)	19 (7.1)
Other LLTs			
Moderate/low intensity statins§ in monotherapy	6 (7.5)	12 (6.3)	18 (6.7)
Omega 3 in monotherapy	5 (6.3)	8 (4.2)	13 (4.8)
Fibrates in monotherapy	1 (1.3)	4 (2.1)	5 (1.9)
Bile acid sequestrants in monotherapy		1 (0.5)	1 (0.4)
Other LLT combinations	2 (2.5)	5 (2.6)	7 (2.6)

Legend: LLT=lipid lowering therapy; *reimbursement criteria= "prior treatment with high intensity statin agent and ezetimibe, or ezetimibe monotherapy in case of statins intolerance, for at least 6 months; ^ high intensity statins: atorvastatin (40 and 80 mg), rosuvastatin (20 and 40 mg); § moderate/low intensity statin: atorvastatin (10 and 20 mg), rosuvastatin (5 and 10 mg), simvastatin, lovastatin, pravastatin, fluvastatin

Fig 2 - Temporal trend of PCSK9 inhibitor starting in Tuscany Region from July 2017 to June 2018



Tab 2 - PCSK9 inhibitor patterns of use in the first 6 months of treatment

PCSK9 inhibitors' new users	Evolocumab N (%) 175 (100)	Alirocumab N (%) 91 (100)	Total N (%) 266 (100)
Adherence (PDC)[a]			
<75	34 (19.4)	19 (20.9)	53 (19.9)
≥75	141 (80.6)	72 (79.1)	213 (80.1)
Persistence and continuityb			
Persistent for 6 months	127 (72.6)	68 (74.7)	195 (73.3)
Interruption followed by new dispensing	36 (20.6)	15 (16.5)	51 (19.2)
Interruption after more than one dispensing	9 (5.1)	7 (7.7)	16 (6.0)
Interruption after the first dispensing	3 (1.7)	1 (1.1)	4 (1.5)
Switch[c]	1 (0.6)	0 (0.0)	1 (0.4)

Legend: PDC= Proportion of Days Covered (i.e. the sum of days covered by medications divided by number of days in the follow-up period);
a) PDC≥75 was considered as indicator of good adherence to the treatment.
b) Persistence has been defined as absence of a gap longer than 30 days between the end of the duration of a dispensing and the new dispensing (discontinuation) or end of follow-up (interruption)..
c) Change between the two active substances during the follow-up

CONCLUSIONS

During the first-year of availability, **the administration of PCSK9-inhibitors appears below expectations**. Patients were mainly in secondary prevention and had been previously persistent to LLTs. During follow-up, **the PCSK9-inhibitor monotherapy showed high adherence and persistence**. This real-world study sets the stage for future longer-term investigations useful to improve our knowledge on the appropriateness, drug access and public healthcare sustainability of PCSK9-inhibitors.

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