Use of inclisiran in a real-world setting: results from the italian Cholinet registry

C. Basile1, P. Gargiulo1, C. Indolfi2, N.D. Brunetti3, G. Musumeci4, G. Casu5, G. Galasso6, F. Varbella7, A. Cesaro8, G. Patti9, S. Carugo10, F. Marzano1, S. Paolillo1, P.A. Merlini11, P. Perrone-Filardi1

1Federico II University Hospital, Naples, Italy
2Magna Graecia University of Catanzaro, Catanzaro, Italy
3University of Foggia, Foggia, Italy
4Mauriziano Umberto Hospital, Turin, Italy
5Sassari University Hospital, Sassari, Italy
6San Giovanni di Dio and Ruggi d’Aragona University Hospital, Salerno, Italy
7Degli Infermi Hospital, Rivoli, Italy
8AO dei Colli - Monaldi Hospital, Naples, Italy
9University of Eastern Piedmont, Novara, Italy
10University of Milan, Milan, Italy
11ASST Great Metropolitan Niguarda, Milan, Italy
On behalf of Cholinet investigators

Funding Acknowledgements: None.

Background: Real world data indicate that PCSK9 inhibitors (PCSK9i) are started in very high-risk patients at higher LDL cholesterol (LDL-C) values than those recommended by guidelines. Different reimbursement rules may have an impact on access to injectable therapy among different countries. In Italy, reimbursement of injectable lipid lowering therapies (LLT) (i.e., PCSK9i and inclisiran) has been recently allowed for very high risk patients with LDL-C levels >70 mg/dl while on statin/ezetimibe LLT or statin intolerant, and, thereafter, inclisiran has been introduced in clinical practice. No data are available on inclisiran real world use in Italy and on the impact of new reimbursement rules on patient access to inclisiran.

Purpose: Cholinet (Cholesterol inclisiran Italian network) is an Italian multicenter prospective phase 4 registry involving 21 Italian centers, designed to assess efficacy, safety, adherence and persistence, as well characteristics of very high risk patients with atherosclerotic CV disease (ASCVD) and/or familial hypercholesterolemia (FH) receiving inclisiran.

Methods: From November 2022 through February 2023, the Cholinet registry enrolled patients receiving inclisiran due to elevated LDL-C levels in Italian centers as part of their medical therapy. Baseline characteristics, concomitant therapies, blood chemistry, were recorded at the time of first prescription and at follow-up.

Results: We enrolled 105 patients (14% FH, 30% female, mean age 64 years) receiving inclisiran according to standard clinical practice. 37 of them reached 3 months follow up (i.e., time of first reinjection dose) and none of them missed the reinjection dose. At the time of inclisiran first prescription median LDL-C was 96.6 mg/dl and reached 48.8 mg/dl at the time of 3 months observation (49% reduction). In patients with ASCVD median LDL-C at baseline was 90.4 mg/dl and 44.4 mg/dl at follow-up (51% reduction). In patients with FH median LDL-C at baseline was 177.4 mg/dl and 109.5 mg/dl at follow-up (38% reduction). Of 105 patients enrolled, 92 patients (88%) were on LLT. Heterogeneity was found on the LDL-C reduction across our cohort (Figure 1) (Shapiro-Wilk test \( p < 0.05 \)) that appeared to be influenced by background LLT (Kruskal-Wallis rank for previous PCSK9i exposure \( p = 0.0028 \), for background LLT \( p = 0.0435 \) (Figure 2), but not by baseline LDL-C levels (ANOVA \( p = 0.06 \)). LDL-C target was achieved in 21 (66%) of 32 patients receiving background LLT and in 2 (40%) of 5 patients who did not. No patient reported side effects.

Conclusion: These preliminary results from the Cholinet registry show that, in a context of facilitated reimbursement access, inclisiran is introduced at substantially lower baseline LDL-C values than previously reported for PCSK9i, reflecting a favorable change in clinical practice. Inclisiran effectively and safely reduces LDL-C in patients with ASCVD or FH, with some heterogeneity that was associated with background LLT.
Kernel density plot, LDL-C % reduction
Stratified Kernel density plot

Density

% Change in LDL-C

Previous PCSK9i therapy
No previous PCSK9i therapy
Not on background LLT
On background LLT