inklisiranu. Priemerná zmena hladín lipidového profilu bola vypočítaná u každého pacienta, ktorý absolvoval tretiu dávku inklisiranu.

Výsledky: Liečba inklisiranom bola schválená pre 36 pacientov, z toho 27 s aterosklerotickým ochorením koronárnych artérií a 9 po prekonaní cievnej mozgovej príhody. Súbor zahŕňal 1 pacienta intolerantného na statíny, 28 pacientov na maximálnej dávke statínov a 7 na zníženej dávke. Po 3 mesiacoch sa hladina LDL-C znížila o 57,5 %, hsCRP na 1,2 mg/dl a lipoproteín(a) o 14,3 ± 6,4 %. Bezpečnostné výsledky boli v súlade s klinickými štúdiami – mierna bolesť v mieste vpichu sa vyskytla u 26 pacientov a chrípkové príznaky u 3 pacientov.

Záver: Inklisiran preukázal účinné zníženie hladín LDL-C a hsCRP, pričom výsledky mierne prevýšili klinické štúdie. Redukcia lipoproteínu(a) sa medzi pacientmi líšila. Bezpečnostný profil bol v súlade s očakávaniami, čo potvrdzuje potenciál inklisiranu pre širšie klinické využitie.

Kľúčové slová: inklisiran, LDL-C, hsCRP, lipoproteín(a), cieľové hodnoty.

Introduction

A significant advancement in both primary and secondary prevention of cardiovascular (CV) diseases, which remain the leading cause of mortality and morbidity. According to recent data, CV mortality in Europe accounts for 45 % of all deaths in women and 39 % in men, respectively (1). In Slovakia, CV diseases account for 45.3 % of all causes of death, while in the Czech Republic, they represent 38 %, reflecting the European trend (2, 3).

Hyperlipidemia is the most significant risk factor for the development and progression of atherosclerotic CV diseases (ASCVD). Lowering LDL cholesterol (LDL-C) levels is a fundamental pillar in the management of ASCVD. It has long been established that each 1 mmol/L reduction in LDL-C leads to a 22% decrease in the relative risk of CV events over a period of 5 years (4). In patients at very high CV risk, rapidly achieving target LDL-C levels, particularly in those following an acute coronary syndrome or revascularization, is crucial for stabilizing atherosclerotic plaques (5).

Inclisiran is a new long-acting parenteral lipid-lowering agent. This small interfering RNA (siRNA) inhibits hepatic production of proprotein convertase subtilisin/kexin type 9 (PCSK9). PCSK9 is a protease that, upon binding to the LDL receptor, induces its degradation in lysosomes. By inhibiting PCSK9 production, the degradation of LDL receptors is reduced, their recycling increases, and this results in a reduction in LDL-C (6).

The efficacy and safety of inclisiran are evaluated in the ORION clinical trial program. Phase II and III studies have shown that inclisiran reduces LDL-C by approximately 50 % with dosing once every six months and is effective in patients with ASCVD as well as those at high CV risk, including patients with heterozygous familial hypercholesterolemia (FH) (7,8). Currently, additional Phase III clinical trials are underway to provide evidence on the long-term safety and efficacy of inclisiran, as well as the ORION-4 study, which focuses on evaluating its impact on CV morbidity and mortality. Results are expected in 2026 (9).

Despite the absence of these data, inclisiran was approved by the European Medicines Agency at the end of 2020. It is indicated as an adjunct to dietary measures for individuals with heterozygous FH or non-familial hypercholesterolemia or mixed dyslipidemia at very high CV risk with manifest atherosclerotic disease, where existing high-intensity lipid-lowering therapy has proven insufficiently effective.

The aim of this study was to describe the effectiveness of inclisiran in a group of patients with very high CV risk according to current indication criteria in Slovakia, as well as to highlight specific aspects of managing these patients.

Methods

Between March 2023 and August 2024, 36 patients (25 men and 11 women, average age 60.2 ± 7.1 years) were included in this open cohort prospective registry. These patients had very high CV risk. Among them, 75 % had clinical atherosclerotic coronary artery disease (ASCAD).

Inclisiran was prescribed to patients with FH or mixed dyslipidemia who had a very high CV risk and clinical evidence of ASCAD, and whose LDL-C levels remained above 2.5 mmol/L despite receiving intensive lipid-lowering therapy. It was also recommended for individuals with heterozygous FH whose LDL-C levels exceeded 3.1 mmol/L despite high intensity therapy. Intensive lipid-lowering therapy was defined as the maximum tolerated dose of statins (atorvastatin or rosuvastatin) combined with ezetimibe, or in cases of statin intolerance, treatment with ezetimibe alone. Statin intolerance was identified if a patient could not tolerate at least two different statins, resulting in their discontinuation.

Prior to initiating treatment, each patient had a lipid profile done (including total cholesterol, LDL-C, HDL-C, triglycerides, and lipoprotein (Lp(a)), and liver parameters (alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyltransferase (GGT), as well as inflammatory markers (high-sensitivity C-reactive protein (hsCRP)) assessed, along with screening for other modifiable CV risk factors such as smoking, hypertension, diabetes, and obesity.

All patients met the Slovak criteria for insurance-covered PCSK9 inhibitor treatment with inclisiran (Figure 1). Inclisiran was initially administered as a 284 mg subcutaneous injection, followed by a second dose after three months, and then a third dose after six months. A lipid profile was measured before each injection. In addition, at each visit, clinical information was recorded, including any ASCVD events or side effects. The therapy was discontinued if patients were non-compliant or if the treatment was ineffective, defined as less than a 40% reduction in LDL-C by the sixth to ninth month, or failure to reach the LDL-C target.

All patients underwent standard cardiology examinations. From an ethical standpoint, this study adhered to standard treatment protocols and was conducted as an observational study based on anonymous processing of results from routine examinations after patients