

Lacking Observance of the Guidelines on Dyslipidaemias As Possible Reason for Low LDL-C Goal Attainment in Patients at High and Very High Cardiovascular Risk

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OBJECTIVE

Several studies have clearly demonstrated the causative role of increased plasma concentrations of LDL-C in the process of atherosclerotic plaque formation (1)(2)(3). These findings have been reflected in the updated guidelines for the management of dyslipidaemias, proposing new stringent LDL-C goals and treatment algorithm (4). Although the evidence is quickly translated into the guidelines, there is still a large gap between recommendations and real clinical practice (5). The objective of the study was to investigate the adherence of Czech cardiologists to the dyslipidaemias guidelines, especially in the management of patients with high- and very-high cardiovascular risk.

METHODS

- ❖ A non-interventional retrospective cross-sectional multicentric study involving 46 specialists (internal medicine and cardiology) treating patients at risk of ASCVD in the Czech Republic
- ❖ Anonymous patient data were collected from medical records of 450 adults between June 2021 and January 2022 including demographics, clinical outcomes, medical history, lipid lowering therapy (LLT) and other medications (inclusion criteria: patient at the very high cardiovascular risk; aged ≥ 18 years and with prescribed LLT at least one year prior to the enrollment in the study)
- ❖ In addition to patient data the physicians were to complete a general questionnaire on their personal therapeutic preferences regarding the management of ASCVD

Results

Achievement of the LDL-C goals defined by the 2019 European Society of Cardiology/European Atherosclerosis Society Guideline

- Only 20.5% of the patients reached the 2019 LDL-C goals – 19.4% of very high-risk patients and 28.1% of high-risk patients (Fig.1). If the less strict 2016 goals were considered, it would be 38%, and 72.4%, respectively.
- Surprisingly, in up to 61.5% of patients at very high risk who did not meet the LDL-C goals, the physicians stated subjective satisfaction with the treatment outcomes and did not consider any therapeutic regimen change (Fig. 1).
- 91.8% of all participating patients were recognized by their physicians as adherent to pharmacotherapy.

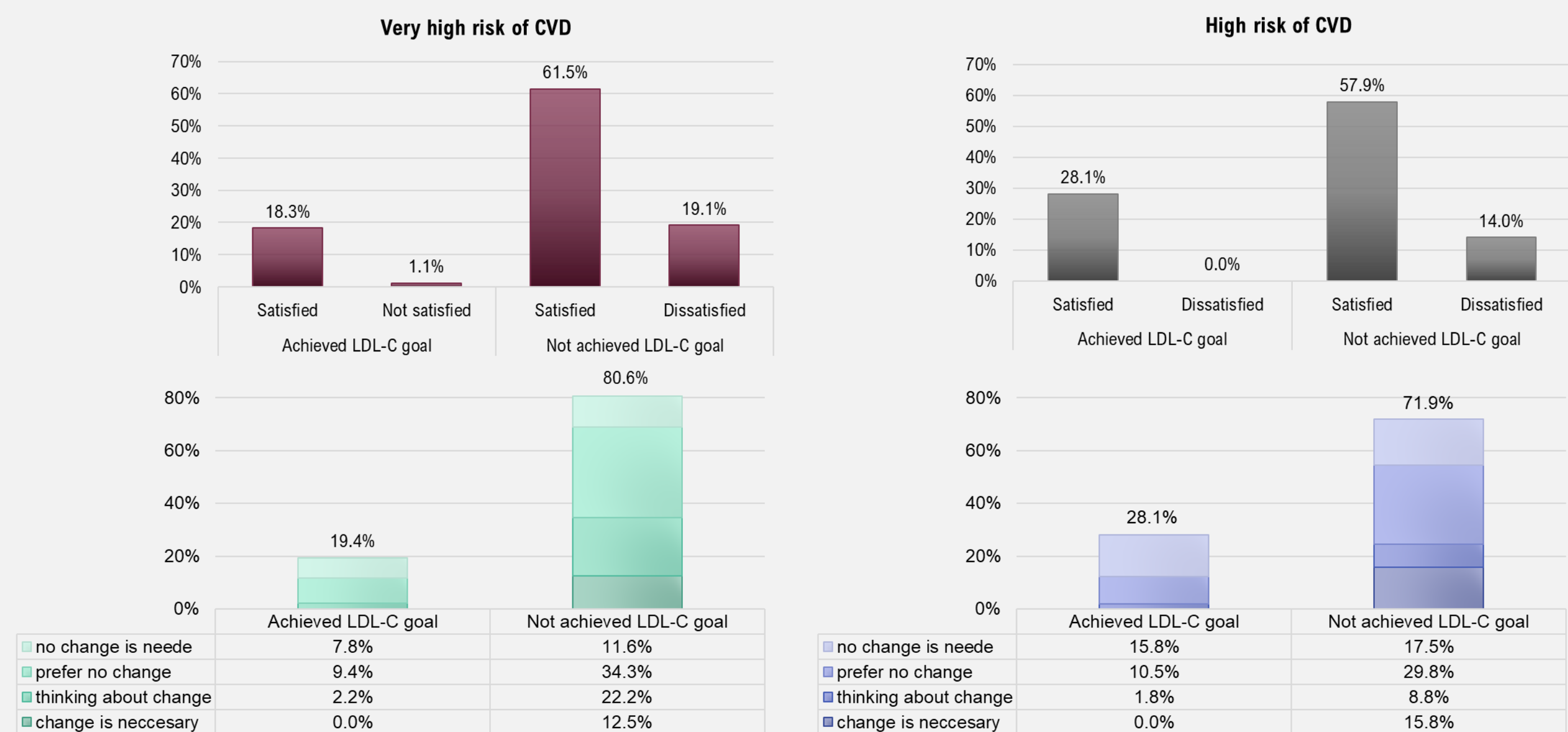


Fig. 1 Achievement of the 2019 ESC/EAS Guidelines LDL-C goals in the context of physicians' subjective perception of treatment outcomes in patients at high risk and very high risk. The satisfaction was evaluated based on grouped responses to the question: *How satisfied are you with the outcome of treatment for this patient? (completely satisfied/rather satisfied/rather dissatisfied/completely dissatisfied)*. The physicians' attitudes towards the change of treatment comprise from responses to the question: *Given the overall success of the patient's treatment, are you considering a change in pharmacotherapy? (Change is necessary/ I'm thinking about the change/ I lean towards the existing treatment/ There is definitely no need to change the treatment)*.

Physicians' attitudes in the management of patient with dyslipidaemias

- As an objective measure of LLT efficacy, 73.9% of the physicians selected LDL-C, 23.9% CV risk reduction, and 2.2% total lipid profile. LDL-C was considered as the primary target of LLT by 65.2% of physicians, while 23.9% of them stated the CV risk reduction as the main target.
- Most of the physicians (61%) preferred a slow and careful up-titration of the dose, which is contradictory to the guidelines. Only 17% of the physicians increased the statin dose or combined/changed for a more effective LLT to achieve the LDL-C goals (Fig. 2).
- Although two thirds of the doctors were convinced that specialized centres may provide better care for patients, up to 74% of them recommend patients to the centre only occasionally/exceptionally and 88.8% stated that they prefer to treat patients by themselves.
- In only 23% of patients who objectively met the reimbursement criteria for PCSK9i treatment based on our stratification, the physicians were considering referral to the centre, while for up 22.5% of those patients they did not state another benefit in the treatment resulting from referring to the centre (Fig. 3).

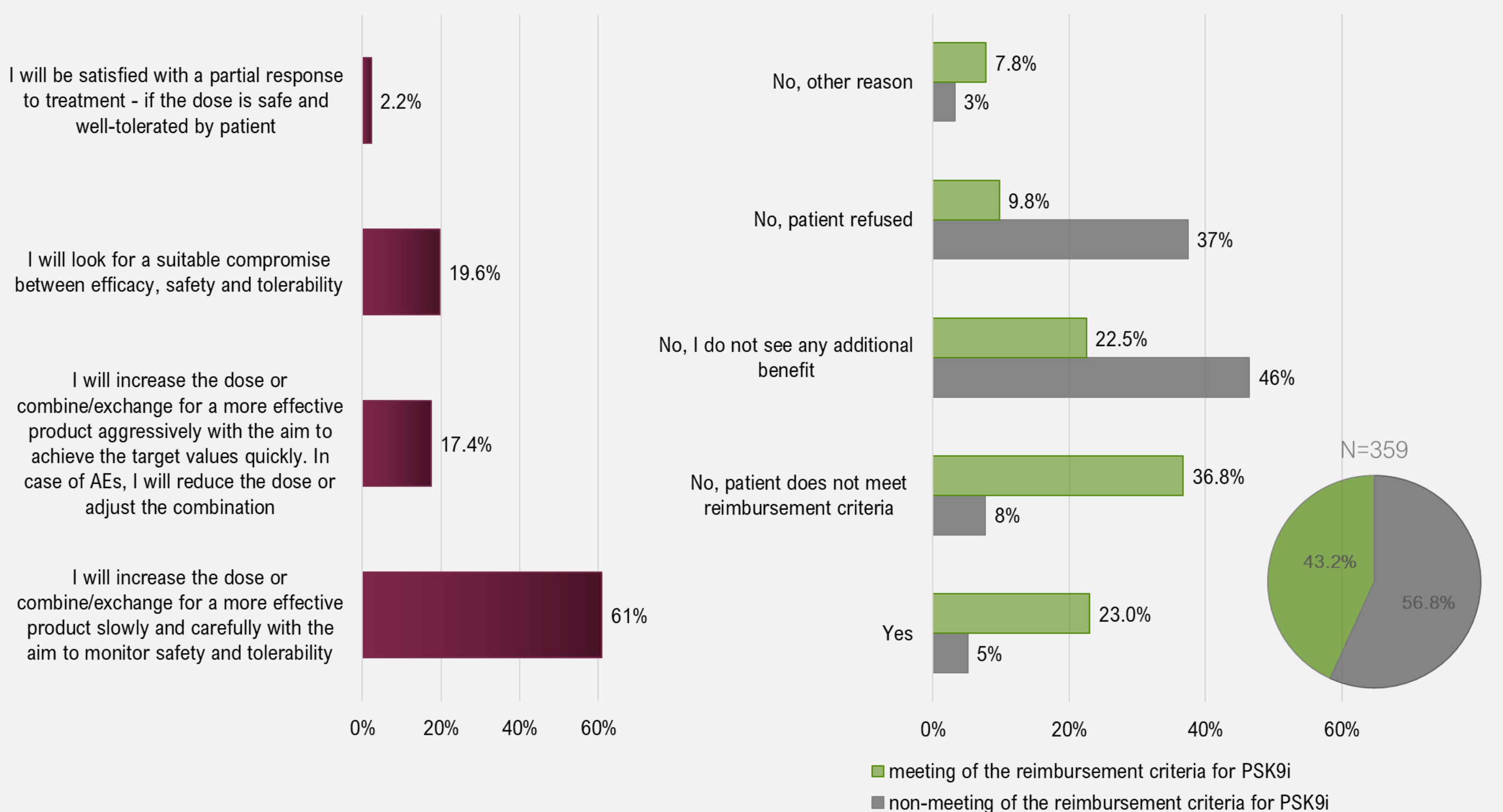


Fig. 2 Physicians attitudes in case of insufficient patient response to the lipid-lowering therapy. The percentage represents the portion of responds to the questions: 1. *Which of the following statements best describes your attitude in case of insufficient response to treatment with lipid-lowering drugs?* N=46

Fig. 3 Sub-group of patients diagnosed with familial hypercholesterolemia and patients after cardiovascular event(s) stratified according to the meeting/non-meeting of the reimbursement criteria for treatment with PCSK9 inhibitors. A sub-group of patients with FH and at a very high risk after CV event(s) (N=359) were analyzed and stratified according to the meeting of the official reimbursement criteria for PCSK9 inhibitors treatment (Pie chart). The bar chart represents portion of physicians' responds to the questions *Would you consider referring the patient to the centre for PCSK9i treatment?* for the sub-groups.

Utilization of lipid-lowering therapy

- LLT of analyzed patients consisted of 48.3% statin monotherapy, 43.1% statins in combination with ezetimibe, 3.8 % statins in combination with fenofibrate, and 4.8% of non-statin LLTs including PCSK-9 inhibitors.
- High-intensity statins and statins with ezetimibe were predominantly used in patient at very high risk, especially in patients with a history of a CV event.
- Among very high-risk patients receiving statin monotherapy, the 2019 LDL-C goal attainment was 5.4% and 11.4% at moderate- and high-intensity statin therapy, respectively, and 22.7% for those receiving the combination of ezetimibe and statin. Among the high-risk patients, it was 11.4% and 8.6%, respectively, and 52.9% for the statin-ezetimibe combination. 3 of 7 patients receiving PCSK9i reached the LDL-C goal (Fig. 4).

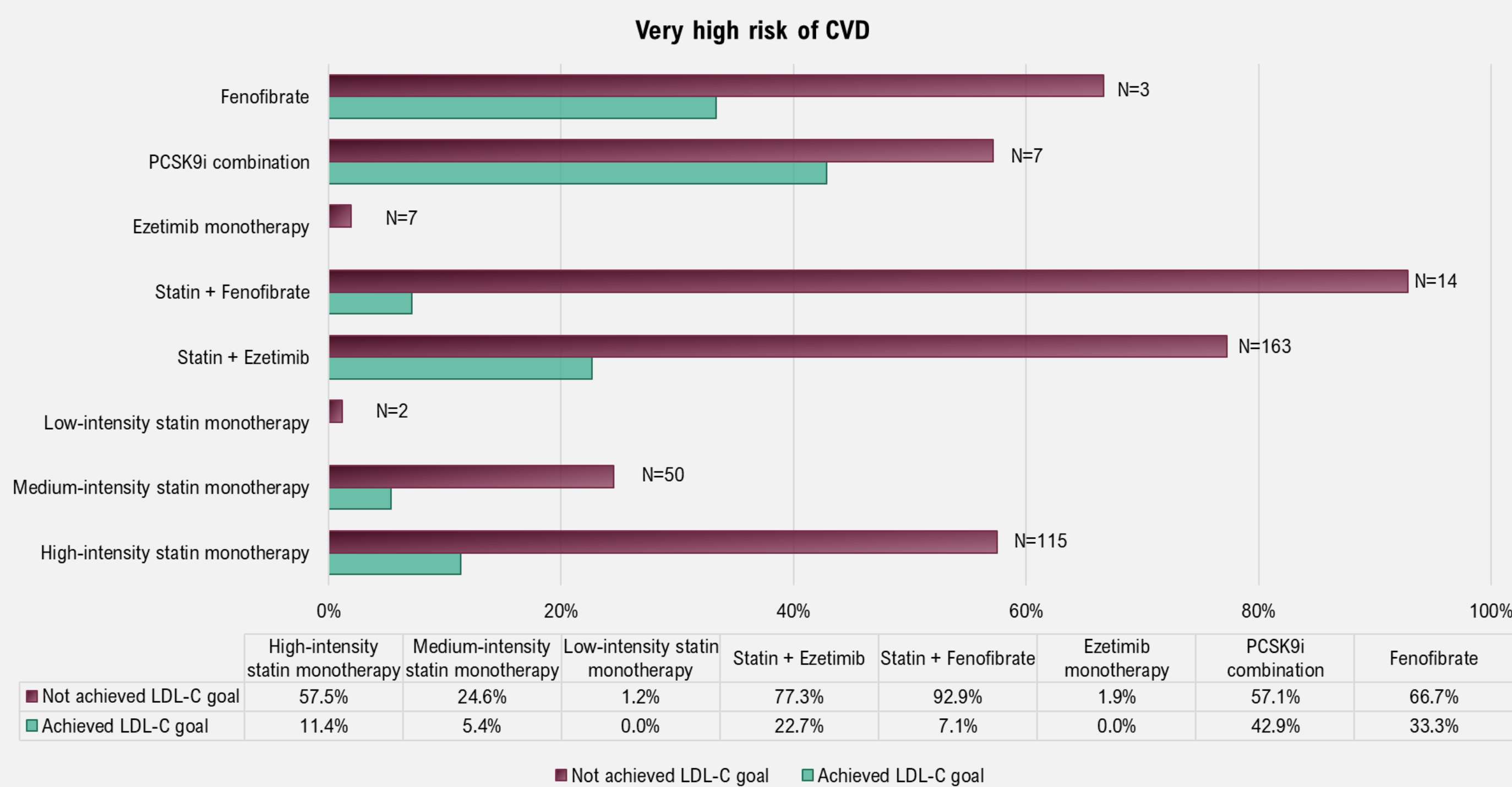


Fig. 4 LDL-C goals attainment summarized by LLT regimens in in patients at very high risk. N is the number of patients receiving the corresponding type of LLT.

The theoretical therapy efficacy, e.g., the LDL-C value that could be achieved in ideal conditions by titrating the statin dosage or/and by adding ezetimibe to the regimen, was calculated for those patients who did not attain the recommended goals and were not treated with maximum statin doses/ezetimibe combination (patients with known adverse events/statin intolerance were excluded). The percentage of the maximum reduction of LDL-C was calculated as it was shown previously in randomized clinical trials for each drug/combination (6)(7).

High risk of CVD			Current achievement of LDL-C goal		Would Achieve LDL-C goal		
Current therapy	Therapeutical potencial	Max. possible reduction of LDL-C	Yes	No	Yes	No	
High-intensity statin monotherapy	+ Ezetimib	-20%	3	12	7	8	+ 28% in total
Medium-intensity statin monotherapy	High- intensity statin + Ezetimib	-26%	4	14	12	6	
Low-intensity statin monotherapy	High-intensity statin + Ezetimib	-50%	0	1	1	0	
Statin + Ezetimib	High-intensity statin	-6%	9	7	10	6	
Statin + Fenofibrate	+ Ezetimib	-20%	0	2	2	0	

Very high risk of CVD			Current achievement of LDL-C goal		Would Achieve LDL-C goal		
Current therapy	Therapeutical potencial	Max. possible reduction of LDL-C	Yes	No	Yes	No	
High-intensity statin monotherapy	+ Ezetimib	-20%	19	96	38	77	+ 13.9% in total
Medium-intensity statin monotherapy	High- intensity statin + Ezetimib	-26%	9	41	27	23	
Low-intensity statin monotherapy	High-intensity statin + Ezetimib	-50%	0	2	0	2	
Statin + Ezetimib	High-intensity statin	-6%	37	120	43	114	
Statin + Fenofibrate	+ Ezetimib	-20%	1	13	1	13	
Ezetimib monotherapy	+ High- intensity statin	-50%	0	7	7	0	

Table 1 Therapy potential. The number of patients in both risk groups who could reach the 2019 ESC/EAS Guidelines LDL-C goals if the intensity of their LLT was maximized. The percentage of the maximum reduction of LDL-C was calculated as it was shown previously in randomized clinical trials for each drug/combination (6)(7).

CONCLUSIONS

Among risky patients receiving LLT, with relatively high treatment adherence, the LDL-C goal attainment is very low and LLT utilization is sub-optimal. The analysis of the physicians' attitudes toward dyslipidaemias management indicates non-optimal adherence of clinicians to the guidelines as one of possible reasons for low LDL-C goal attainment.