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Bridging Guidelines and Practice: Expert Insights on Early Rosuvastatin–Ezetimibe Combination Therapy

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ABSTRACT

Background: Cardiovascular disease remains the leading cause of mortality globally and in India, driven by a high burden of dyslipidemia and premature coronary artery disease. Despite widespread statin use, attainment of recommended LDL-C targets in real-world practice remains suboptimal. Contemporary ESC/EAS, CSI, and LAI guidelines advocate aggressive LDL-C goals (<55 mg/dL) and early combination therapy, underscoring the need for expert-informed real-world insights.
Materials and Methods: This expert-opinion analysis incorporated structured polling conducted across five advisory board forums involving approximately 50 practicing cardiologists from India. Fourteen predefined electronic polling questions assessed LDL-C targets, treatment preferences in primary and secondary prevention, observed lipid-lowering responses, and treatment duration.
Results: In primary prevention, most respondents supported rosuvastatin 40 mg plus ezetimibe for very-high or extreme-risk patients, while statin monotherapy remained the most common initial approach overall. In hospitalized ASCVD patients, rosuvastatin–ezetimibe was the preferred regimen (44%), typically initiated at LDL-C <55 mg/dL (63%). Similar trends were observed post-PCI, where combination therapy predominated and <55 mg/dL was the principal threshold (68%). The regimen was widely prescribed, achieving typical LDL-C reductions of 40–50%, and was commonly continued beyond 12 months, including extended or lifelong use in selected high-risk patients.
Conclusion: Expert polling indicates substantial alignment between real-world cardiology practice and guideline-recommended aggressive lipid management. Rosuvastatin–ezetimibe therapy is widely adopted across ASCVD and post-PCI settings, with reported effectiveness consistent with clinical trial data, supporting an evolving shift toward early and sustained combination lipid-lowering strategies.

Keywords: *Dyslipidemias; Cholesterol, LDL; Statins; Ezetimibe; Combination Drug Therapy.*

INTRODUCTION

Cardiovascular disease (CVD) continues to be the leading cause of mortality worldwide and remains a major contributor to morbidity in India, where the burden is disproportionately high due to premature and aggressive coronary artery

disease (CAD) [1,2]. Dyslipidemia, particularly elevated low-density lipoprotein cholesterol (LDL-C), is a well-established and modifiable causal factor in the development and progression of atherosclerotic cardiovascular disease (ASCVD) [3].

Large population-based studies from India, most notably the ICMR-INDIAB study, highlight the extensive prevalence of dyslipidemia across both urban and rural populations. Nearly 79% of adults were found to have at least one abnormal lipid parameter, with elevated LDL-C (≥130 mg/dL) observed in approximately 11–21% of individuals, low high-density lipoprotein cholesterol (HDL-C) in nearly two-thirds of the population, and hypertriglyceridemia exceeding 30% in several regions [4,5]. These findings underscore not only the magnitude but also the heterogeneity of lipid abnormalities in the Indian population, reinforcing the urgent need for effective and scalable lipid-lowering strategies to reduce ASCVD risk.

Despite widespread statin use, real-world LDL-C goal attainment remains suboptimal, particularly among patients at very-high cardiovascular risk. Observational studies consistently demonstrate that only a minority of high-risk patients achieve guideline-recommended LDL-C targets in routine clinical practice, resulting in persistent residual cardiovascular risk attributable to inadequate lipid lowering [6–8]. This gap between evidence-based recommendations and real-world outcomes represents a critical challenge in contemporary cardiovascular prevention.

In response, contemporary lipid management guidelines have progressively emphasized more aggressive LDL-C targets and the importance of achieving these goals early in the disease course. The 2019 European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) dyslipidemia guidelines recommend an LDL-C target of <55 mg/dL, with at least a 50% reduction from baseline, for very-high-risk individuals, with consideration of even lower targets in those at extreme risk [9].

Indian guidelines from the Cardiological Society of India (CSI) and the Lipid Association of India (LAI) are closely aligned with these recommendations, endorsing early and intensive lipid lowering in patients with established ASCVD, including those presenting with acute coronary syndromes (ACS) and those undergoing percutaneous coronary intervention (PCI) [10,11]. Importantly, these guidelines increasingly support early initiation of combination lipid-lowering therapy rather than delayed, stepwise escalation of statin monotherapy when substantial LDL-C reduction is required.

From a pharmacological standpoint, this strategy is supported by robust evidence. Doubling the statin dose typically results in only a modest incremental LDL-C reduction of approximately 6–8%, whereas the addition of ezetimibe provides an additional 10–15% LDL-C reduction by inhibiting intestinal cholesterol absorption, thereby complementing hepatic cholesterol synthesis inhibition [12–14]. This additive mechanism enables more pronounced LDL-C lowering without a proportional increase in statin-related adverse effects and is particularly relevant in elderly patients or those with limited tolerance to very high statin doses.

Clinical outcomes data further reinforce the role of combination therapy. The IMPROVE-IT trial demonstrated that adding ezetimibe to statin therapy following ACS resulted in incremental LDL-C lowering and a significant reduction in major adverse cardiovascular events compared with statin monotherapy [15]. In addition, intravascular imaging studies have shown favorable effects of intensive lipid-lowering strategies on atherosclerotic plaque burden and composition, including plaque regression and stabilization, supporting a disease-modifying effect beyond lipid reduction alone [16,17]. Despite this expanding evidence base and strong guideline endorsement, meaningful gaps persist between recommendations and their implementation in real-world Indian clinical settings. These challenges highlight the need for expert opinion to contextualize clinical trial evidence and guideline recommendations, address practical barriers to implementation, and provide pragmatic insights tailored to populations with a high burden of residual cardiovascular risk. Integrating structured expert perspectives with published literature may help delineate best practices and inform more effective strategies for LDL-C target attainment and ASCVD risk reduction in routine clinical care.

METHODS

This analysis was conducted as an expert opinion study incorporating structured polling during five cardiologist advisory board forums. Total 50 practicing cardiologists from across India participated, including clinicians actively involved in the management of dyslipidemia, atherosclerotic cardiovascular disease (ASCVD), and post–percutaneous coronary intervention (PCI) patients. The objective was to capture contemporary real-world perspectives on lipid-lowering strategies, particularly the use of statin–ezetimibe combination therapy, and to contextualize these opinions with current guideline recommendations and published evidence.

During each forum, a set of 14 predefined polling questions was administered in real time using electronic polling tools. The questions covered LDL-C targets prompting initiation of combination therapy, preferred lipid-lowering strategies in primary and secondary prevention, observed LDL-C reduction with statin–ezetimibe combinations, clinical confidence in early combination therapy, and real-world utilization patterns including duration of therapy. Poll responses were recorded anonymously and pooled across all five sessions. Results are presented descriptively as percentages of responding

cardiologists for each option. As the study was based on expert opinion and anonymized polling data without patient-level information or interventions, formal ethics committee approval was not required.

RESULTS

The aggregated polling responses across the expert forums are summarized in Table 1.

Table 1. Polling Results from Expert Forums on Lipid-Lowering Strategies

Polling Questions	Polling Result
Which risk category would you use the combination of Ezetimibe + Rosuvastatin 40 mg for primary prevention?	• Extreme-risk / very-high-risk: **60%** • High-risk: **22%** • Would not use upfront: **18%**
What percentage reduction in LDL-C do you typically observe after initiating Rosuvastatin 40 mg + Ezetimibe 10 mg in dyslipidemia?	• 51–70% reduction: **53%** • 40–50% reduction: **28%** • >70% reduction: **19%**
For primary prevention, which lipid-lowering strategy do you prefer to initiate?	• Statin monotherapy: **41%** • Rosuvastatin 20 mg + Ezetimibe: **33%** • Rosuvastatin 10 mg + Ezetimibe: **28%** • Rosuvastatin 40 mg + Ezetimibe: **8%**
In what percentage of ASCVD patients do you prescribe Rosuvastatin 40 mg + Ezetimibe?	• >50% of patients: **42%** • 25–50%: **33%** • <25%: **25%**
In what percentage of post-PCI patients do you prescribe Rosuvastatin 40 mg + Ezetimibe?	• >50% of patients: **43%** • 25–50%: **32%** • <25%: **25%**
For how long do you usually continue combination lipid-lowering therapy post-PCI?	• >12 months: **47%** • 6–12 months: **33%** • ≤6 months: **20%**

Primary Prevention: Expert Opinion and Supporting Evidence

In the primary prevention setting, cardiologists demonstrated a distinctly risk-stratified approach toward the use of high-intensity rosuvastatin–ezetimibe combination therapy. When queried regarding upfront initiation of ezetimibe with rosuvastatin 40 mg, 60% of respondents supported its use in extreme-risk or very-high-risk primary prevention patients, underscoring a clear preference for reserving this regimen for individuals with the highest anticipated cardiovascular risk. A notable proportion of clinicians favored its use in high-risk patients, whereas a minority indicated that they would defer combination therapy in primary prevention. This pattern closely reflects contemporary guideline recommendations, which advocate early and intensive LDL-C lowering predominantly in individuals at very-high or extreme cardiovascular risk who are unlikely to achieve recommended LDL-C targets with statin monotherapy alone [1–3].

Clinicians also reported robust LDL-C reductions with rosuvastatin 40 mg plus ezetimibe in patients with dyslipidemia, with the most frequently observed response being a 51–70% reduction in LDL-C, while other respondents described either more modest or more pronounced lipid lowering. These real-world observations are concordant with findings from randomized clinical trials and pooled analyses, including the EXPLORER study, which demonstrated significantly greater LDL-C reduction and higher goal attainment with rosuvastatin 40 mg plus ezetimibe compared with rosuvastatin monotherapy ($p<0.001$) [4]. Similar benefits across different statin intensities have been reported in studies such as GRAVITY and other rosuvastatin–ezetimibe trials, reinforcing the efficacy of combination therapy when substantial LDL-C reduction is required [5–7].

Correspondingly, when selecting initial therapy in primary prevention, 41% of cardiologists preferred statin monotherapy, while 33% chose rosuvastatin 20 mg plus ezetimibe, 28% rosuvastatin 10 mg plus ezetimibe, and 8% rosuvastatin 40 mg plus ezetimibe, reflecting a balanced, evidence-based approach that escalates treatment intensity according to baseline risk and LDL-C burden.

Secondary Prevention (ASCVD): Expert Opinion and Supporting

Evidence Preferred Lipid-Lowering Strategy in Hospitalized ASCVD Patients

Among hospitalized patients with established ASCVD, cardiologists demonstrated a clear preference for early initiation of combination lipid-lowering therapy as shown in figure no. 1. Rosuvastatin plus ezetimibe emerged as the most commonly initiated regimen (44%)**,** underscoring its dominant role in contemporary secondary prevention practice. Other lipid-lowering strategies included atorvastatin combined with ezetimibe, high-intensity statin monotherapy, and alternative approaches, which were selected less frequently. Overall, these findings indicate a strong inclination toward combination therapy over statin monotherapy.

This real-world practice pattern aligns closely with guideline recommendations. The 2019 ESC/EAS guidelines and the 2025 focused update support early intensification of lipid-lowering therapy during index hospitalization for ASCVD and ACS, including statin–ezetimibe combination therapy when LDL-C targets are unlikely to be achieved with statin

monotherapy alone [1,2]. Similar guidance from the CSI and LAI emphasizes early combination therapy in high-risk Indian patients to enable timely LDL-C target attainment [3,4].

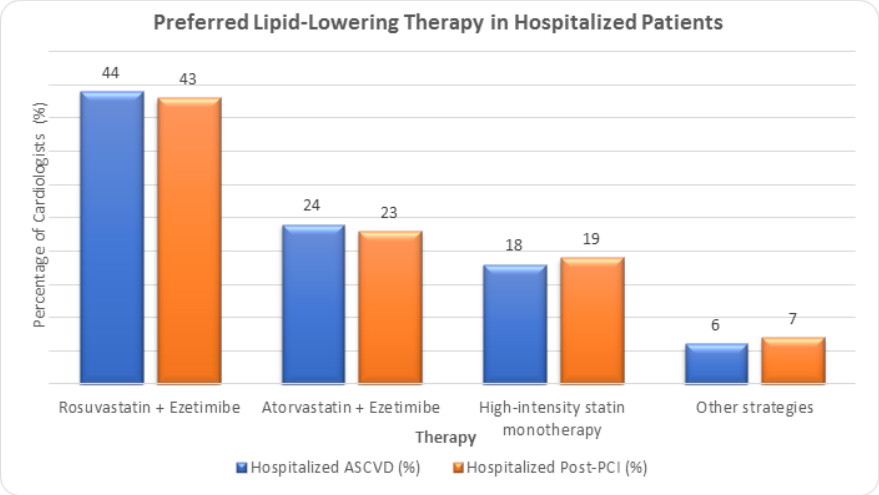

Figure 1. Percentage of cardiologists indicating preferred lipid-lowering strategies in hospitalized ASCVD and post-PCI patients

LDL-C Targets Prompting Initiation of Combination Therapy

When queried on LDL-C thresholds prompting initiation of combination therapy in hospitalized ASCVD patients, the majority of cardiologists reported initiating combination therapy at an LDL-C target of <55 mg/dL (63%), indicating a strong preference for aggressive lipid lowering in very-high-risk patients. A smaller proportion of clinicians selected higher LDL-C thresholds for initiating combination therapy (Fig 2). This distribution demonstrates close alignment with guideline-recommended LDL-C targets for secondary prevention.

Contemporary ESC/EAS guidelines recommend an LDL-C target of <55 mg/dL with ≥50% reduction from baseline in patients with established ASCVD, a strategy also endorsed by CSI and LAI for secondary prevention [1–4]. Evidence indicates that earlier attainment of lower LDL-C levels after an index ASCVD event is associated with reduced risk of recurrent cardiovascular events [5].

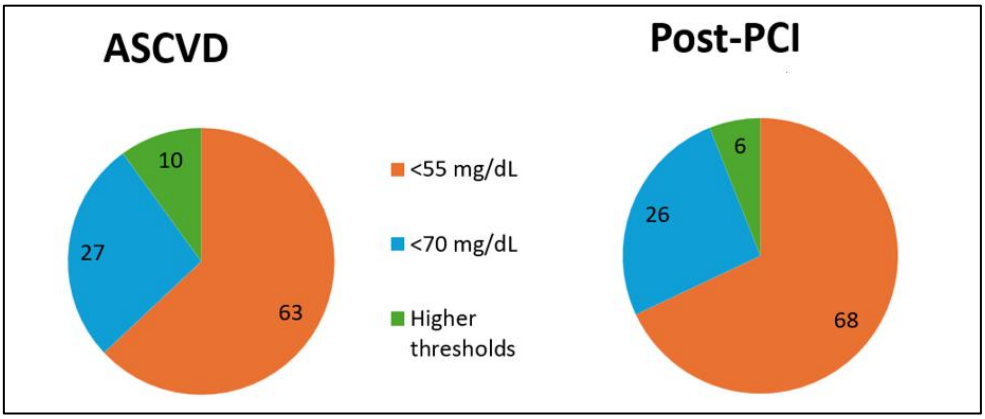

Figure 2. Percentage of cardiologists indicating LDL-C thresholds for initiation of combination lipid-lowering therapy in hospitalized ASCVD and post-PCI patients

Expert Agreement on Early Rosuvastatin–Ezetimibe Combination Therapy

A strong consensus emerged regarding the perceived benefit of early combination therapy. When asked whether early initiation of rosuvastatin plus ezetimibe in ASCVD patients improves LDL-C target achievement and long-term outcomes, a clear majority of respondents strongly agreed (73%), while the remaining clinicians expressed agreement, with only a negligible proportion reporting neutral or dissenting views (Fig 3). This reflects a high level of clinical confidence in the role of early combination therapy in secondary prevention.

The IMPROVE-IT trial demonstrated that adding ezetimibe to statin therapy after ACS provides greater LDL-C reduction and lowers cardiovascular events compared with statin alone [6]. Meta-analyses in ACS populations further confirm that early ezetimibe use with high-intensity statins results in sustained LDL-C lowering and improved outcomes [5,7].

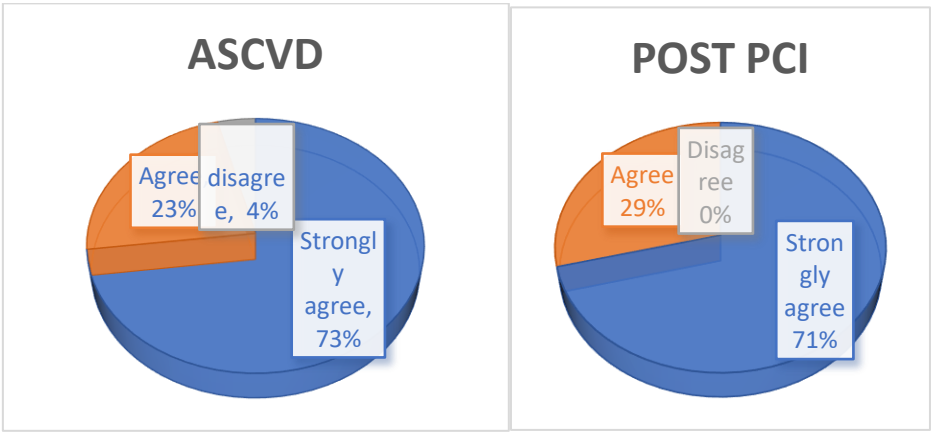

Figure 3. Level of agreement among cardiologists regarding early rosuvastatin–ezetimibe combination therapy in ASCVD and post-PCI settings

Real-World Utilization of Rosuvastatin 40 mg Plus Ezetimibe in ASCVD

The largest proportion of cardiologists reported prescribing rosuvastatin 40 mg plus ezetimibe in more than half of their ASCVD patients (42%), indicating substantial real-world uptake of this high-intensity combination in secondary prevention. Other clinicians reported more selective use across a smaller proportion of their ASCVD population.

Consistent with this utilization pattern, clinicians reported clinically meaningful LDL-C reductions with statin–ezetimibe combination therapy. Following initiation of rosuvastatin 40 mg plus ezetimibe, the most commonly observed response was a 40–50% reduction in LDL-C (48%), while other respondents described greater degrees of LDL-C lowering. Similarly, with rosuvastatin 10/20 mg plus ezetimibe, a 61-70% reduction in LDL-C was most frequently reported (53%), with a subset of clinicians observing more pronounced reductions and others reporting more modest responses (Fig 4). These real-world observations closely mirror findings from randomized trials such as EXPLORER and pooled analyses demonstrating superior LDL-C lowering and higher target attainment with statin–ezetimibe combination therapy compared with statin monotherapy [8–10].

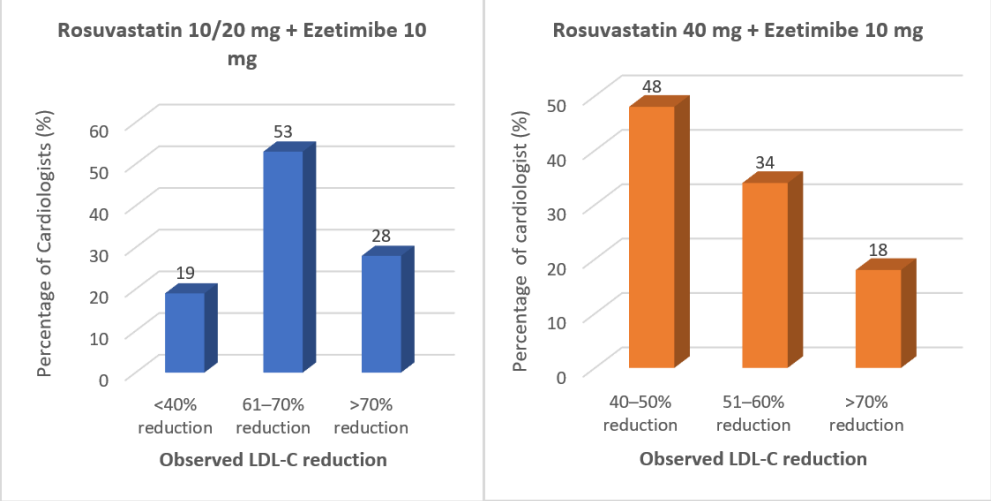

Figure 4. Percentage of cardiologist-reported LDL-C reduction with rosuvastatin 40 mg and rosuvastatin 10/20 mg plus ezetimibe in ASCVD patients

Secondary Prevention in Post-PCI Patients: Expert Opinion and Supporting Evidence

Preferred Lipid-Lowering Strategy Following PCI

In patients hospitalized following PCI, cardiologists demonstrated a clear preference for early combination lipid-lowering therapy. Rosuvastatin plus ezetimibe emerged as the most commonly initiated regimen (43%), underscoring its predominant role in immediate post-PCI management (Fig 1). This pattern reflects recognition of the very-high residual cardiovascular risk in the post-PCI period and the need for early, effective LDL-C reduction.

This approach is consistent with ESC/EAS, CSI, and LAI guidelines recommending early intensification with statin–ezetimibe therapy in very-high-risk post-PCI patients when LDL-C targets are not achieved [4].

LDL-C Targets Prompting Combination Therapy Post-PCI

When queried on LDL-C thresholds prompting initiation of combination therapy after PCI, the majority of cardiologists reported initiating combination therapy at an LDL-C target of <55 mg/dL (68%), indicating a strong preference for aggressive lipid lowering in this very-high-risk population. Smaller proportions of clinicians selected higher LDL-C thresholds (Fig 2). Overall, this distribution demonstrates close alignment with guideline-recommended LDL-C targets following coronary intervention.

ESC/EAS and CSI guidelines recommend an LDL-C target of <55 mg/dL with ≥50% reduction from baseline in post-ACS and post-PCI patients, and early achievement of these targets is associated with improved outcomes and lower risk of recurrent cardiovascular events [1,5,6].

Rosuvastatin 40 mg Plus Ezetimibe as Preferred Therapy Post-PCI

A strong expert consensus was observed regarding the preferred high-intensity lipid-lowering regimen following PCI. The majority of respondents strongly supported rosuvastatin 40 mg plus ezetimibe 10 mg as the preferred regimen (71%), while the remaining clinicians expressed agreement, with no dissenting views reported (Fig 4). This finding indicates broad acceptance of this combination therapy in post-PCI secondary prevention.

Randomized trials and meta-analyses demonstrate superior LDL-C reduction and higher target attainment with rosuvastatin–ezetimibe versus statin monotherapy, with early ezetimibe initiation also associated with sustained LDL-C lowering and reduced recurrent cardiovascular events in very-high-risk patients [6–9].

Real-World Utilization and Duration of Therapy After PCI

In routine clinical practice, the largest proportion of cardiologists reported prescribing rosuvastatin 40 mg plus ezetimibe in more than half of their post-PCI patients (43%), indicating substantial real-world uptake of this combination in secondary prevention. Other clinicians reported more selective use across a smaller proportion of their post-PCI population. With respect to treatment duration, continuation of combination therapy beyond 12 months was most commonly reported (47%), while shorter durations were chosen less frequently, reflecting a tendency toward prolonged intensive lipid-lowering in patients with persistent residual risk.

Support for extended therapy is provided by intravascular ultrasound studies demonstrating significant plaque regression with rosuvastatin–ezetimibe therapy, including approximately 15% reduction in plaque burden and 46% reduction in necrotic core over 12 months, indicating enhanced plaque stabilization following PCI [10].

Expert Panel Perspectives on Translating Evidence into Clinical Practice

Beyond the quantitative polling results, advisory board discussions provided valuable insight into how emerging evidence and updated guidelines are being applied in routine clinical practice. Experts emphasized that recent guideline revisions have not only lowered recommended LDL-C targets but have also shifted the therapeutic approach toward achieving these targets earlier and sustaining them over time. Experts repeatedly noted that delaying treatment intensification by gradually increasing statin doses often results in late achievement of LDL-C targets in high-risk patients. In this context, early initiation of statin–ezetimibe combination therapy was viewed as a pragmatic strategy to overcome inertia and facilitate timely attainment of guideline-recommended LDL-C goals.

With respect to treatment duration following PCI, experts generally favored continuation of statin–ezetimibe combination therapy for at least 6–12 months in patients at very-high or extreme cardiovascular risk. Several participants observed that in patients with persistent very-high cardiovascular risk, combination therapy is commonly continued long term, including lifelong use in selected cases, based on LDL-C levels, risk profile, and tolerability. This approach reflects increasing acceptance of sustained intensive lipid lowering as a key component of secondary prevention, particularly in the Indian context characterized by premature CAD, high cardiometabolic risk, and recurrent events.

CONCLUSION

Across expert forums, cardiologists demonstrated strong alignment with contemporary guidelines advocating aggressive LDL-C targets, particularly <55 mg/dL, in very-high and extreme-risk patients. Early initiation of statin–ezetimibe combination therapy was consistently preferred over statin monotherapy in hospitalized ASCVD and post-PCI settings. Rosuvastatin 40 mg plus ezetimibe 10 mg was associated with substantial real-world LDL-C reductions, comparable to those reported in clinical trials. Most experts favored initiation during index hospitalization and continuation for at least 6–12 months, with extended or lifelong use in selected high-risk patients. Collectively, these findings highlight a clear shift toward early and sustained combination lipid-lowering therapy to address residual cardiovascular risk in routine clinical practice.

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