Combination therapy in ACS management: myth or reality?

Dr Mohamed Abdel Ghany
Professor of Cardiology
Cairo University

Persistent Risk in Post-ACS Patient

CV Mortality is the killer #1 in the world

- Every 40 seconds, someone dies from Cardiovascular Disease
- Every 4 minutes, someone dies from Stroke
- 18 million people across the globe died from heart disease in 2015
- Over 400 million men and women have a kind of cardiovascular illness

1. Published: May, 17, 2017 Source: The Journal of the American College of Cardiology
2. Published: January 25, 2017 Source: American Heart Association Statistical Update 2017
Patient Risk Stratification

Is the extra dimension to identify which patients are at risk.

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Moderate Risk</th>
<th>High Risk</th>
<th>Very high Risk</th>
<th>Extreme Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ASCVD!! but Marked elevated risk factor (↑LDL, ↑BP)</td>
<td>DM</td>
<td>Moderate CKD (GFR 30-59)</td>
<td>Score &lt; 1% (≥1% - &lt; 5%) (≥5% - &lt;10%)</td>
<td>Score ≥ 10%</td>
</tr>
<tr>
<td>&lt;115 mg/dL</td>
<td>&lt;115 mg/dL</td>
<td>&lt;100 mg/dL or 50% if baseline</td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
</tbody>
</table>
How far we are from **adhering**
to clinical guidelines?

Only **30.6%** of all 6792 CHD patients achieved
target value of LDL < (70 mg/dL)

Only **25.7%** of all 3867 ACS patients achieved
target value of LDL < (70 mg/dL)
Only 19.3% of all 6648 CHD patients achieved target value of LDL < (70 mg/dL)

Among patients discharged on high-intensity statins, only 26.6% achieved LDL < (70 mg/dL)

- Cardiologists and primary care physicians are knowing the concept of preventive cardiology and treatment of LDL-C to the target values, but not doing what should be done.

- It's not only that adequate statin type and dosage should be used but that much more often combined lipid lowering therapy should be used in order to achieve LDL-C. This could be a combination of a statin and ezetimibe.
High intensity statin is Not Enough, what comes next???
Cholesterol Absorption Inhibitor

- Ezetimibe localizes at the brush border of the small intestine and inhibits the intestinal absorption of dietary and biliary cholesterol (by selectively blocking the transporter protein “Niemann-Pick C1-Like1” NPC1L1) leading to a decrease in the delivery of intestinal cholesterol to the liver.

- It does not interfere with the absorption of triglycerides, fat-soluble vitamins, fatty acids, or bile acids.

Ezetimibe and Statins Have Complementary Mechanisms of Action\(^1\)

Together, ezetimibe in combination with a statin provides:

1. Reduction of hepatic cholesterol
2. Increased LDL receptor expression
3. Increased clearance of plasma LDL-C

Inhibition of absorption
Ezetimibe alone

Inhibition of synthesis
Statin alone

Dual Inhibition
Ezetimibe/Statin

CHANGE OF SYNTHESIS AND ABSORPTION MARKERS


MEAN LDL-C LOWERING%

10% 20% 30% 40% 50%

LDL-C

20%

30-45%

As high as 60%

Combination with Ezetimibe: Significantly greater LDL-C decrease vs. statin titration

Significantly greater LDL-C reduction across the dose range of Ezetimibe/Simvastatin vs. Atorvastatin

Mean LDL-C reductions were 6% to 11% greater than the corresponding doses of atorvastatin (p<0.001 for each comparison).

Effects of different doses of Ezetimibe/Simvastatin vs. Rosuvastatin on LDL-C reduction

The change in LDL-C from baseline to week 6 was 55.8% for ezetimibe/simvastatin 10/20–10/80 mg, which was significantly greater than the 51.6% reduction for rosuvastatin 10–40 mg (p<0.001).

*p<0.001 vs. corresponding dose of Rosuvastatin

Adapted from Ballantyne CM et al Am Heart J 2005;149:464–473

Adapted from Catapano et al. CURRENT MEDICAL RESEARCH AND OPINION 2016
DOI: 10.1185/030079906X132721
Does **Ezetimibe** provide additional benefits for such patients?

**IMP**roved **R**eduction of **O**utcomes: **V**ytorin **E**fficacy **I**nternational **T**rial

A Multicenter, Double-Blind, Randomized Study to Establish the Clinical Benefit and Safety of Vytorin (Ezetimibe/Simvastatin Tablet) vs Simvastatin Monotherapy in High-Risk Subjects Presenting With Acute Coronary Syndrome
Study Design

Patients stabilized post ACS ≤ 10 days:
LDL-C 50–125*mg/dL (mean LDL-C is 95 mg/dL)

N=18,144

Standard Medical & Interventional Therapy

Simvastatin
40 mg

Uptitrated to Simvastatin 80 mg if LDL-C > 79 (adapted per FDA label 2011)

Follow-up Visit Day 30, every 4 months

Duration: Minimum 2 ½-year follow-up (at least 5250 events)

Primary Endpoint: CV death, MI, hospital admission for UA, coronary revascularization (≥ 30 days after randomization), or stroke

Cannon CP AHJ 2008;156:826-32; Califf RM NEJM 2009;361:712-7; Blazing MA AHJ 2014;168:205-12

LDL-C at Entry and Projected On-Treatment LDL-C

Patients at Entry | Median LDL-C
---|---
All patients | 95 mg/dL (2.5 mmol/L)
Lipid-lowering naive | 104 mg/dL (2.7 mmol/L)
Prior lipid-lowering therapy | 80 mg/dL (2.1 mmol/L)

Treatment Arm | Projected Mean On-Treatment LDL-C
---|---
Ezetimibe/simvastatin 10/40 mg | <55 mg/dL (<1.4 mmol/L)
Placebo/simvastatin 40 mg | <70 mg/dL (<1.8 mmol/L)

*Values are aggregated across the still-blinded treatment groups.

*Simvastatin could be titrated to 80 mg in both arms if LDL-C was >79 mg/dL, titration stopped per June 2011 protocol amendment.

**LDL-C and Lipid Changes**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>LDL-C</th>
<th>TC</th>
<th>TG</th>
<th>HDL</th>
<th>hsCRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simva</td>
<td>69.9</td>
<td>145.1</td>
<td>137.1</td>
<td>48.1</td>
<td>3.8</td>
</tr>
<tr>
<td>EZ/Simva</td>
<td>53.2</td>
<td>125.8</td>
<td>120.4</td>
<td>48.7</td>
<td>3.3</td>
</tr>
<tr>
<td>Δ in mg/dL</td>
<td>-16.7</td>
<td>-19.3</td>
<td>-16.7</td>
<td>+0.6</td>
<td>-0.5</td>
</tr>
</tbody>
</table>

Median Time avg 69.5 vs. 53.7 mg/dL

**Primary Endpoint On Treatment**

HR 0.924 CI (0.868, 0.983)

p=0.012

NNT= 38

Simva — KM 32.4%
2079 events

EZ/Simva — KM 29.8%
1932 events

7.6% Treatment effect

Primary Endpoint: CV death, MI, hospital admission for UA, coronary revascularization (≥ 30 days after randomization), or stroke
**Individual Cardiovascular Endpoints and CVD/MI/Stroke**

<table>
<thead>
<tr>
<th>Event</th>
<th>HR 0.6</th>
<th>HR 1.0</th>
<th>HR 1.4</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause death</td>
<td>0.99</td>
<td>15.3</td>
<td>15.4</td>
<td>0.782</td>
</tr>
<tr>
<td>CVD</td>
<td>1.00</td>
<td>6.8</td>
<td>6.9</td>
<td>0.997</td>
</tr>
<tr>
<td>CHD</td>
<td>0.96</td>
<td>5.8</td>
<td>5.7</td>
<td>0.499</td>
</tr>
<tr>
<td>MI</td>
<td>0.87</td>
<td>14.8</td>
<td>13.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.86</td>
<td>4.8</td>
<td>4.2</td>
<td>0.052</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>0.79</td>
<td>4.1</td>
<td>3.4</td>
<td>0.008</td>
</tr>
<tr>
<td>Cor revasc ≥ 30d</td>
<td>0.95</td>
<td>23.4</td>
<td>21.8</td>
<td>0.107</td>
</tr>
<tr>
<td>UA</td>
<td>1.06</td>
<td>1.9</td>
<td>2.1</td>
<td>0.618</td>
</tr>
<tr>
<td>CVD/MI/stroke</td>
<td>0.90</td>
<td>22.2</td>
<td>20.4</td>
<td>0.003</td>
</tr>
</tbody>
</table>

*7-year event rates (%)

Ezetimibe/Simva Better
Simva Better

**Reduction in Total (First and Recurrent) Cardiovascular Events with Ezetimibe/Simvastatin compared with Simvastatin Alone post ACS in the IMPROVE-IT Trial**

Sabina A. Murphy, Christopher Cannon, Robert Giugliano, Michael Blazing, Thomas Musliner, Andrew Tershakovec, Jennifer White, Kelly Im, Naveen Deenadayalu, Haral Darius, Witold Ruzyllo, Andrew Tonkin, Uma Kher, Robert Califf, Eugene Braunwald

On behalf of the IMPROVE IT Investigators
Total Primary Endpoint Events

- Ezetimibe: 4562
- Simvastatin Alone: 4983

Total Events
- RR 0.91
- P=0.007

Additional Events
- RR 0.88
- (0.79-0.98)

1st Event
- HR 0.936
- P=0.016

Secondary Events
- 421
- 251
- 170
- 12%
- 6.4%

Safety and efficacy of long-term very low achieved LDL-C in the IMPROVE IT trial

IMProved Reduction of Outcomes: Vytorin Efficacy International Trial

RP Giugliano, SD Wiviott, MA Blazing, SA Murphy, J Zhou, JA White, TA Musliner, AJ Tershakovec, CP Cannon, E Braunwald
Methods

- Primary analysis: 4 groups by LDL-C at month 1
  1) <30 mg/dL (<0.8 mM/L)  
  2) 30-<50 mg/dL (0.8-1.3 mM/L)  
  3) 50-<70 mg/dL (1.3-1.8 mM/L)  
  4) ≥70 mg/dL (1.8 mM/L)

- Excluded pts who had an event prior to month 1

- Main analyses: pooled results across 2 Rx groups

- 9 Safety events evaluated:
  - AE->drug discon - AST/ALT>3x - Cancer
  - Myalgias with CK↑ - Neurocognitive - CHF-> Rehosp
  - Heme stroke - Gall bladder AEs - Non-CV death

- Primary efficacy endpoint* and other efficacy analyses adjusted for baseline differences

*CV death, MI, UA, coronary revasc after 30 days, stroke

Achieved LDL-C at 1 month

Median: 56 [43-71] mg/dL

<table>
<thead>
<tr>
<th>LDL-C range</th>
<th># pts</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30 mg/dL</td>
<td>975</td>
<td>6%</td>
</tr>
<tr>
<td>30 - &lt;50 mg/dL</td>
<td>4603</td>
<td>31%</td>
</tr>
<tr>
<td>50 - &lt;70 mg/dL</td>
<td>5552</td>
<td>36%</td>
</tr>
<tr>
<td>≥70 mg/dL</td>
<td>4061</td>
<td>26%</td>
</tr>
</tbody>
</table>

4 Groups by LDL-C at 1 mth

LDL-C achieved at Month 1 (mg/dL)
**Safety — ITT**

- No statistically significant differences in cancer or muscle- or gallbladder-related events

<table>
<thead>
<tr>
<th>Event</th>
<th>Simva n=9077 %</th>
<th>EZ/Simva n=9067 %</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT and/or AST≥3x ULN</td>
<td>2.3</td>
<td>2.5</td>
<td>0.43</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>1.5</td>
<td>1.5</td>
<td>0.96</td>
</tr>
<tr>
<td>Gallbladder-related AEs</td>
<td>3.5</td>
<td>3.1</td>
<td>0.10</td>
</tr>
<tr>
<td>Rhabdomyolysis*</td>
<td>0.2</td>
<td>0.1</td>
<td>0.37</td>
</tr>
<tr>
<td>Myopathy*</td>
<td>0.1</td>
<td>0.2</td>
<td>0.32</td>
</tr>
<tr>
<td>Rhabdo, myopathy, myalgia with CK elevation*</td>
<td>0.6</td>
<td>0.6</td>
<td>0.64</td>
</tr>
<tr>
<td>Cancer* (7-yr KM %)</td>
<td>10.2</td>
<td>10.2</td>
<td>0.57</td>
</tr>
</tbody>
</table>

*Adjudicated by Clinical Events Committee  % = n/N for the trial duration

The addition of Ezetimibe to Simvastatin vs. Simvastatin alone did not increase the risk of new onset diabetes
Ezetimibe has a Confirmed safety profile

Thrombolysis In Myocardial Infarction (TIMI) Risk Score
Are independent predictors of the endpoint of primary interest for atherothrombotic risk stratification “composite of CV death, MI, or ischemic stroke”

To identify a post-ACS population of patients at higher risk who have the greatest potential for benefit from the addition of ezetimibe to statin therapy in the IMPROVE-IT trial

http://dx.doi.org/10.1016/j.jacc.2016.11.070
Addition of Ezetimibe to Simvastatin in patients at highest risk

Addition of Ezetimibe to Simvastatin in patients at highest risk

19% RRR
with NNT=16

Acute coronary syndromes

The benefit of adding ezetimibe to statin therapy in patients with prior coronary artery bypass graft surgery and acute coronary syndrome in the IMPROVE-IT trial

Alon Eisen¹, Christopher P. Cannon¹, Michael A. Blazing², Erin A. Bohula², Jeong-Gun Park², Sabina A. Murphy¹, Jennifer A. White², Robert P. Giugliano¹, and Eugene Braunwald¹, on behalf of the IMPROVE-IT (IMProved Reduction of Outcomes: Vytorin Efficacy International Trial) Investigators

¹TPS Study Group, Cardiovascular Division, Brigham and Women’s Hospital and Harvard Medical School, 350 Longwood Avenue, 1st Floor Offices, Boston, MA 02115, USA; and "Duke Clinical Research Institute, Durham, NC, USA

Received 8 May 2016; revised 8 July 2016; accepted 8 August 2016; online publication-ahead-of-print, 28 August 2016
Addition of Ezetimibe to Simvastatin in patients with prior CABG

14.6% RRR with NNT=11

IMPROVE-IT results modified the clinical guidelines
2. Clinical ASCVD with Co-morbidities:
DM, Recent acute ASCVD event, ASCVD event on statin, Baseline LDL-C ≥190 mg/dL, Uncontrolled risk factors, Elevated Lp(a), CKD

- Treat with maximal tolerated statin
- Achieve at least ≥50% LDL-C reduction
- If this reduction is not achieved, initiate patient clinician discussion and consider non statins if LDL-C ≥70 mg/dL or non-HDL-C ≥ 100 if diabetic
- Ezetimibe first
- PCSK9 inhibitor next
- If treatment objective achieved, follow lipids
- If not, reassess medication adherence and lifestyle
- Mipomersen, lomitapide and/or LDL apheresis in appropriate patients
**ESC CP Guidelines 2016 – Highlights: Dyslipidaemias**

### Treatment targets

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2011 ESC Dyslipidaemias guidelines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VERY-HIGH CV risk: LDL-c goal &lt;70 mg/dl (1.8 mmol/L) and/or 50% reduction when target cannot be reached</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>HIGH CV risk: LDL-c goal &lt;100 mg/dl (2.5 mmol/L)</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td>MODERATE CV risk: LDL-c goal &lt;115 mg/dl (3.0 mmol/L)</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td><strong>2016 ESC Dyslipidaemias guidelines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VERY-HIGH CV risk: LDL-c goal &lt;70 mg/dl (1.8 mmol/L) and/or 50% reduction if baseline is 70-135 mg/dl (1.8-3.5 mmol/L)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>HIGH CV risk: LDL-c goal &lt;100 mg/dl (2.6 mmol/L) or 50% reduction if baseline is 100-200 mg/dl (2.6-5.1 mmol/L)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>MODERATE CV risk: LDL-c goal &lt;115 mg/dl (3.0 mmol/L)</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

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### Drug combinations

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2011 ESC Dyslipidaemias guidelines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If goal is not reached, statin combination with a cholesterol absorption inhibitor, bile sequestran acid or nicotinic acid should be considered</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td><strong>2016 ESC Dyslipidaemias guidelines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If goal is not reached, statin combination with a cholesterol absorption inhibitor should be considered</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Statin combination with a bile acid sequestrant may be considered</td>
<td>IIb</td>
<td>B</td>
</tr>
</tbody>
</table>
### Table 9.1—Recommendations for statin and combination treatment in people with diabetes

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk factors</th>
<th>Recommended statin intensity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>ASCVD risk factor(s)**</td>
<td>Moderate or high</td>
</tr>
<tr>
<td></td>
<td>ASCVD</td>
<td>High</td>
</tr>
<tr>
<td>40–75 years</td>
<td>None</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>ASCVD risk factors</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>ASCVD</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>ACS and LDL cholesterol ≤50 mg/dL (1.3 mmol/L) or in patients with a history of ASCVD who cannot tolerate high-dose statins</td>
<td>Moderate plus ezetimibe</td>
</tr>
<tr>
<td>&gt;75 years</td>
<td>None</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>ASCVD risk factors</td>
<td>Moderate or high</td>
</tr>
<tr>
<td></td>
<td>ASCVD</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>ACS and LDL cholesterol ≥50 mg/dL (1.3 mmol/L) or in patients with a history of ASCVD who cannot tolerate high-dose statins</td>
<td>Moderate plus ezetimibe</td>
</tr>
</tbody>
</table>

*In addition to lifestyle therapy. **ASCVD risk factors include LDL cholesterol ≥100 mg/dL (2.6 mmol/L), high blood pressure, smoking, chronic kidney disease, albuminuria, and family history of premature ASCVD.
2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

Routine therapies in the acute, subacute and long-term phases (continued)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lipid lowering therapies</strong></td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>It is recommended to start high-intensity statin therapy as early as possible, unless contra-indicated, and maintain it long term.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>An LDL-C goal of (&lt; 1.8 \text{ mmol/L (70 mg/dL)}) or a reduction of at least 50% if the baseline LDL-C is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) is recommended.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>It is recommended to obtain a lipid profile in all STEMI patients as soon as possible after presentation.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td><strong>In patients with LDL-C (\geq 1.8 \text{ mmol/L (\geq 70 mg/dL)}) despite a maximally tolerated statin dose who remain at high risk, further therapy to reduce LDL-C should be considered.</strong></td>
<td>IIa</td>
<td>A</td>
</tr>
</tbody>
</table>
Endocrinologists and American College of Endocrinology

Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease

Writing Committee
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## ASCVD Risk Categories and LDL-C Treatment Goals

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Risk factors/10-year risk</th>
<th>Treatment goals</th>
</tr>
</thead>
</table>
| **Extreme risk** | – Progressive ASCVD including unstable angina in individuals after achieving an LDL-C <70 mg/dL  
– Established clinical cardiovascular disease in individuals with DM, stage 3 or 4 CKD, or HeFH  
– History of premature ASCVD (<55 male, <65 female) | LDL-C (mg/dL) | Non-HDL-C (mg/dL) | Apo B (mg/dL) |
|               |                           | <55             | <80             | <70             |
| **Very high risk** | – Established or recent hospitalization for ACS, coronary, carotid or peripheral vascular disease, 10-year risk >20%  
– DM or stage 3 or 4 CKD with 1 or more risk factor(s)  
– HeFH | <70             | <100            | <80             |
| **High risk** | – ≥2 risk factors and 10-year risk 10%-20%  
– DM or stage 3 or 4 CKD with no other risk factors | <100            | <130            | <90             |
| **Moderate risk** | – ≤2 risk factors and 10-year risk <10%  
– DM or stage 3 or 4 CKD with no other risk factors | <100            | <130            | <90             |
| **Low risk** | – 0 risk factors  
– DM or stage 3 or 4 CKD with no other risk factors | <130            | <160            | NR              |

**Abbreviations:** ACS, acute coronary syndrome; apo, apolipoprotein; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NR, not recommended.

Question: How are different drugs used to treat dyslipidemia?

Statins

- R56. Statin therapy is recommended as the primary pharmacologic agent to achieve target LDL-C goals on the basis of morbidity and mortality outcome trials (Grade A; BEL 1).
- R57. For clinical decision making, mild elevations in blood glucose levels and/or an increased risk of new-onset T2DM associated with intensive statin therapy do not outweigh the benefits of statin therapy for ASCVD risk reduction (Grade A, BEL 1).
- R58. In individuals within high-risk and very high-risk categories, further lowering of LDL-C beyond established targets with statins results in additional ASCVD event reduction and may be considered (Grade A, BEL 1).
- R59. Very high-risk individuals with established coronary, carotid, and peripheral vascular disease, or diabetes, who also have at least 1 additional risk factor, should be treated with statins to target a reduced LDL-C treatment goal of <70 mg/dL (Grade A, BEL 1).
- R60. Extreme risk individuals should be treated with statins or with combination therapy to target an even lower LDL-C treatment goal of <55 mg/dL (Grade A, BEL 1).

Recommendations associated with this question:

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides.
High Intensity Cholesterol Lowering Therapy

Should replace High Intensity Statin Therapy??
Summary and Conclusions

- Although treatment with high intensity statins; still there is a gap in dyslipidemia management in term of patients don’t reach the LDL-C goal & remaining residual CV risk.

- Achieving even lower LDL-C in high risk populations further reduces risk & appears safe.

- In terms of efficacy: the dual inhibition with EZ/statin reaches up to 60% reduction in LDL.

- In terms of C.V. outcomes, Ezetimibe to reduce LDL-C have proven CV benefit up to 19% RRR in “CV death, MI, or ischemic stroke”.
Therefore, Ezetimibe-Statin combination is now recommended by guidelines for very high / extreme patients.