Ezetimibe Consistently Reduces Low Density Lipoprotein Cholesterol with Little Interindividual Variability Post-ACS

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Background

- Ezetimibe reduces LDL-C and CV events when added to statin therapy.

Background

• There is significant interindividual variability in LDL-C reduction with statin use.

• PCSK9i have demonstrated more consistent LDL-C reduction, with little interindividual variability.

• Whether interindividual variability in LDL-C reduction exists with ezetimibe has not been described in a large study.
Objective

1. To assess the interindividual variability in % LDL-C reduction with the addition of ezetimibe to statin therapy.

2. To model the probability of meeting ACC/AHA and ESC/EAS guideline recommended lipid targets according to randomization LDL-C with the addition of ezetimibe to statin therapy.
Methods: Study Population

Patients stabilized post ACS ≤ 10 days
LDL-C 50-125 mg/dL (or 50-100 mg/dL if prior lipid-lowering Rx)

N=18,144

Standard Medical & Intervventional Therapy

Placebo / Simvastatin
40 mg

Ezetimibe / Simvastatin
10 / 40 mg

Median follow-up: 6 years
Methods: Cohort Selection and Analysis

• LDL-C levels were obtained at randomization and 4 months.
• Excluded patients (n=3174)
  • Missing randomization (n=259) or 4-month LDL-C (n=2109)
  • Not on treatment (n=806)
• Rank-ordered placebo-subtraction was performed based on % change in LDL-C at 4 months from randomization.
• The probability of achieving an LDL-C within guideline targets at 4 months based on randomization LDL-C was modeled using the rank-ordered % change.
**Baseline Characteristics**

<table>
<thead>
<tr>
<th>% or median [IQR]</th>
<th>Study Population (N=14,972)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>62 [56-70]</td>
</tr>
<tr>
<td>Female sex</td>
<td>23</td>
</tr>
<tr>
<td>Caucasian</td>
<td>84</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>28 [25-31]</td>
</tr>
<tr>
<td>Statin Naïve</td>
<td>67</td>
</tr>
<tr>
<td>Diabetes</td>
<td>26</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>33</td>
</tr>
<tr>
<td>Prior MI</td>
<td>20</td>
</tr>
<tr>
<td>Prior PAD</td>
<td>5.4</td>
</tr>
<tr>
<td>Prior Stroke/TIA</td>
<td>5.6</td>
</tr>
<tr>
<td>Baseline LDL (mg/dL)</td>
<td>80 [65-96]</td>
</tr>
</tbody>
</table>

*No significant differences in characteristics between treatment groups (p= NS for all).*
Placebo-adjusted % LDL-C Reduction

Change in LDL-C, %

0 25 50 75 100

Proportion of Patients (N=7418)

Median = 25%
Median = 37%

Simvastatin/Ezetimibe
Placebo-adjusted % LDL-C Reduction

Change in LDL-C, %

-100 -75 -50 -25 0 25 50 75 100

Proportion of Patients (N=7418)

Simvastatin/Placebo
Simvastatin/Ezetimibe

Median: -21%
Median: -37%
Placebo-adjusted % LDL-C Reduction

Change in LDL-C, %

- Simvastatin/Placebo
- Simvastatin/Ezetimibe
- Simvastatin/Placebo-Adjusted

25th %ile -19%
Median -23%
75th %ile -27%

Proportion of Patients (N=7418)
Probability of Achieving Guideline Lipid Targets with Addition of Ezetimibe

Baseline LDL-C in mg/dL (mmol/L)

% of Population Anticipated to Reach Guideline Target

0% 25% 50% 75% 100%

ACC/AHA Target
(<70 mg/dL or <1.8 mmol/L)
Probability of Achieving Guideline Lipid Targets with Addition of Ezetimibe

Baseline LDL-C in mg/dL (mmol/L)

% of Population Anticipated to Reach Guideline Target

ACC/AHA Target
(<70 mg/dL or <1.8 mmol/L)
Probability of Achieving Guideline Lipid Targets with Addition of Ezetimibe

Baseline LDL-C in mg/dL (mmol/L)

% of Population Anticipated to Reach Guideline Target

50% Anticipated to Reach Guideline Target

91 mg/dL

ACC/AHA Target
(<70 mg/dL or <1.8 mmol/L)
Probability of Achieving Guideline Lipid Targets with Addition of Ezetimibe

ESC/EAS Target
(<55 mg/dL or <1.4 mmol/L)
Probability of Achieving Guideline Lipid Targets with Addition of Ezetimibe

% of Population Anticipated to Reach Guideline Target

Baseline LDL-C in mg/dL (mmol/L)

- 50 (1.3)
- 70 (1.8)
- 90 (2.3)
- 110 (2.8)
- 130 (3.4)

ESC/EAS Target
(<55 mg/dL or <1.4 mmol/L)

60 mg/dL
Probability of Achieving Guideline Lipid Targets with Addition of Ezetimibe

ESC/EAS Target
(<55 mg/dL or <1.4 mmol/L)

Baseline LDL-C in mg/dL (mmol/L)

- 72 mg/dL
- 50 (1.3)
- 70 (1.8)
- 90 (2.3)
- 110 (2.8)
- 130 (3.4)

% of Population Anticipated to Reach Guideline Target

- 0%
- 25%
- 50%
- 75%
- 100%
Probability of Achieving Guideline Lipid Targets with Addition of Ezetimibe

- **Baseline LDL-C in mg/dL (mmol/L)**:
  - 50 (1.3)
  - 70 (1.8)
  - 90 (2.3)
  - 110 (2.8)
  - 130 (3.4)

- **ESc/EAs Target**
  - (<55 mg/dL or <1.4 mmol/L)

- **ACC/AHA Target**
  - (<70 mg/dL or <1.8 mmol/L)

- % of Population Anticipated to Reach Guideline Target:
  - 0%
  - 25%
  - 50%
  - 75%
  - 100%
Conclusions

• Ezetimibe added to a background of statin therapy consistently reduces LDL-C (23% median reduction) with little variability (IQR span of 8%)

• Less than half of all patients with a baseline LDL-C > 91 mg/dL or LDL-C > 72 mg/dL are predicted to meet the ACC/AHA (<70mg/dL) or the ESC/EAS (<55mg/dL) guideline targets, respectively.
  • Additional therapies for further LDL-C reduction should be considered in these patients.
THANK YOU