Acute arterial events across all vascular territories in the FOURIER trial

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Backgrounds

Acute arterial vascular events in the coronary, cerebrovascular, and peripheral beds are oftentimes critical or disabling and represent the most feared manifestations of atherosclerosis.

Objective

To assess the impact of PCSK9 inhibitor, evolocumab on acute arterial events across all vascular territories in patients with established ASCVD.
FOURIER was a randomized trial of the PCSK9 inhibitor evolocumab vs. placebo in 27,564 patients with stable atherosclerosis (prior MI, prior non-hemorrhagic stroke, or symptomatic PAD) and LDL-C≥70 mg/dL on maximally tolerated statin therapy followed for a median of 2.2 years.

### Acute arterial events across all vascular territories

<table>
<thead>
<tr>
<th>Acute coronary events</th>
<th>Acute cerebrovascular events</th>
<th>Acute peripheral vascular events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary death</td>
<td>Ischemic stroke</td>
<td>Acute limb ischemia (ALI)</td>
</tr>
<tr>
<td>MI</td>
<td>TIA</td>
<td>Major amputation</td>
</tr>
<tr>
<td>Urgent coronary revascularization</td>
<td>Urgent cerebral revascularization</td>
<td>Urgent peripheral revascularization</td>
</tr>
</tbody>
</table>
Event curves for acute arterial events by treatment groups

Acute arterial events across all vascular beds

- Placebo
- Evolocumab

Cumulative incidence

HR 0.81 (95% CI 0.74-0.88)
P<0.001

Acute arterial events in individual vascular beds

- Coronary events
  - Placebo
  - Evolocumab
  - HR 0.83 (95% CI 0.75-0.91)
P<0.001

- Cerebrovascular events
  - Placebo
  - Evolocumab
  - HR 0.77 (95% CI 0.65-0.92)
P=0.004

- Peripheral vascular events
  - Placebo
  - Evolocumab
  - HR 0.58 (95% CI 0.38-0.88)
P=0.01

Time since randomization (months)

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Landmark and total events analyses

Landmark analyses for efficacy of evolocumab

Effect of evolocumab on first, recurrent, and total acute arterial events

- **0-12 months**
  - 16% RRR (HR 0.84, 95% CI 0.75-0.95)

- **After 12 months**
  - 24% RRR (HR 0.76, 95% CI 0.67-0.85)

Effect of evolocumab compared to placebo:

- **Total events**
  - **Placebo**: 1961
  - **Evolocumab**: 1476
  - RR 0.76 (95% CI 0.69-0.85), P<0.001

- **Additional events**
  - **Placebo**: 482
  - **Evolocumab**: 263
  - RR 0.65 (95% CI 0.58-0.73)

- **First event**
  - **Placebo**: 994
  - **Evolocumab**: 722
  - RR 0.81 (95% CI 0.74-0.88)

Difference between groups:

- **Placebo**: 485
- **Evolocumab**: 222
Conclusions

✓ Adding the PCSK9 inhibitor evolocumab to statin therapy reduced the risk of acute arterial events across all vascular territories with a robust effect over time on both first events and recurrent events.

✓ These findings indicate a panvascular impact of aggressive lipid-lowering therapy on these acute and clinically meaningful events.