Comment on COMMANDER Thrombotic Events Substudy

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Trials with Warfarin in Heart Failure with Sinus Rhythm

1 Am Heart J 2004:148:157-164
2 Circulation 2009;119:1616-1624

Onze Lieve Vrouwe Gasthuis (OLVG), Amsterdam
KM Estimates for MI and Ischemic Stroke in COMMANDER

Myocardial Infarction

- Rivaroxaban
- Placebo

HR (95% CI) 0.83 (0.63, 1.08)

Ischemic Stroke

- Rivaroxaban
- Placebo

HR (95% CI) 0.64 (0.43, 0.95)
Warfarin vs Aspirin after MI (WARIS-2 (n = 3,630) & ASPECT-2 (n = 999))

Death, MI or stroke

Warfarin vs Aspirin after MI (WARIS-2 (n = 3,630) & ASPECT-2 (n = 999))

Death, MI or stroke

Death, MI or stroke

Death


COMPASS: Primary Endpoint

Primary: CV death, stroke, MI

Rivaroxaban + Aspirin vs. Aspirin  HR: 0.76, 95% CI 0.65-0.86, P=<0.0001
Rivaroxaban vs. Aspirin  HR: 0.90, 95% CI 0.79-1.03, P= 0.12

Cumulative Hazard Rate

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Year</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban + Aspirin</td>
<td>6152</td>
<td>7064</td>
<td>5012</td>
<td>3912</td>
<td>858</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>9117</td>
<td>7824</td>
<td>5662</td>
<td>4062</td>
<td>970</td>
</tr>
<tr>
<td>Aspirin</td>
<td>9126</td>
<td>7866</td>
<td>5866</td>
<td>3866</td>
<td>969</td>
</tr>
</tbody>
</table>

### COMPASS: Primary Endpoint

#### Primary components

<table>
<thead>
<tr>
<th>Outcome</th>
<th>R + A (N=9,152)</th>
<th>A (N=9,126)</th>
<th>Rivaroxaban + Aspirin vs. Aspirin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>CV death</td>
<td>160 (1.7%)</td>
<td>203 (2.2%)</td>
<td>0.78 (0.64-0.96)</td>
</tr>
<tr>
<td>Stroke</td>
<td>83 (0.9%)</td>
<td>142 (1.6%)</td>
<td>0.58 (0.44-0.76)</td>
</tr>
<tr>
<td>MI</td>
<td>178 (1.9%)</td>
<td>205 (2.2%)</td>
<td>0.86 (0.70-1.05)</td>
</tr>
</tbody>
</table>
Conclusions

1. Although COMMANDER HF did not meet its primary endpoint, oral anticoagulation did prevent ischemic endpoints (ischemic stroke and MI).

2. These results underscore the long-term benefit of oral anticoagulation in chronic CAD, as found in the old post-MI trials with warfarin and now in modern times in the recent COMPASS and COMMANDER trials.