Prevention of peptic ulcers with once-daily esomeprazole 40 mg and 20 mg in low-dose acetylsalicylic acid users at gastrointestinal risk: outcome analysis by cardiovascular risk (OBERON)

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Study code: D961FC00003
ClinicalTrials.gov identifier: NCT00441727
Disclosures of interest

• J. Scheiman has received lecture fee(s) from AstraZeneca and consultancy fee(s) from AstraZeneca, Bayer, NiCox, Novartis, Pfizer, Pozen and Takeda

• S. Agewall has received financial research support from AstraZeneca

• L-E. Svedberg, E. Nauclér and P. Nagy are current (or former) employees of AstraZeneca

This study was supported by AstraZeneca R&D, Mölndal, Sweden

Medical writing support was provided by Simone Boniface (inScience Communications, a Wolters Kluwer business) and was funded by AstraZeneca R&D, Mölndal, Sweden
Background

- Continuous low-dose ASA (75–325 mg) is a mainstay therapy in the prevention of secondary CV events\(^1\)
- However, low-dose ASA therapy may be associated with upper GI adverse events\(^2\)–\(^4\)
- These GI events may interrupt continuous low-dose ASA therapy\(^5\) and place the patient at an increased risk of a serious CV event\(^6\)
- The proton pump inhibitor esomeprazole has gastroprotective efficacy in such patients\(^7\),\(^8\)

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7Yeomans \textit{et al.} \textit{Am J Gastroenterol} 2008;103:2465–73.
8Scheiman \textit{et al.} \textit{Heart} 2011;97:797–802.

ASA, acetylsalicylic acid; CV, cardiovascular; GI, gastrointestinal
Objective

• To report a *post-hoc* analysis of the efficacy of esomeprazole 40 mg and 20 mg once daily vs placebo for the prevention of peptic ulcer among patients taking low-dose ASA in the OBERON\(^1\) study, by baseline CV risk factor(s)

\(^1\)Scheiman *et al.* *Heart* 2011;97:797–802.

ASA, acetylsalicylic acid; CV, cardiovascular
OBERON: study design

- International, multicentre (204 sites), double-blind, placebo-controlled, parallel-group study
- 2426 patients negative for *Helicobacter pylori* (screening test) and receiving daily low-dose ASA (75–325 mg) for CV risk management, who were also at risk of peptic ulcer (≥1 GI risk factor):
  - Age ≥65 y
  - Age ≥18 y with history of uncomplicated peptic ulcer(s)
  - Age ≥60 y and naïve to low-dose ASA therapy
  - Age ≥60 y with stable coronary artery disease
  - Age ≥60 y with upper GI symptoms and endoscopic finding of ≥5 gastric and/or duodenal erosions


ASA, acetylsalicylic acid; CV, cardiovascular; GI, gastrointestinal
OBERON: patient exclusion criteria

**Gastrointestinal**
- Peptic ulcer at baseline
- History of peptic ulcer complications, such as bleeding and/or perforation
- Reflux esophagitis at baseline

**Cardiovascular**
- Unstable hypertension
- History of acute coronary syndrome, percutaneous coronary intervention and/or coronary artery bypass graft **within the last 3 months**
- Clinically relevant valvular disease
- Serious cardiac failure (NYHA functional classification II–IV, ejection fraction <40%)
- Cerebrovascular accident **within the last 3 months**
- Unstable diabetes mellitus (stable controlled diabetes was acceptable)

OBERON: study design

- Esomeprazole 20 mg once daily (n=804)
- Esomeprazole 40 mg once daily (n=817)
- Placebo (n=805)

Endoscopy
Month: 0
2 (± 4 days)
4 (± 4 days)
6 (± 7 days)

OBERON: primary endpoint

- Endoscopically-confirmed peptic ulcer during the 6-month treatment period
  - Ulcer defined as punched-out defect in the mucosa with a sharply demarcated margin measuring ≥3 mm over its largest diameter

- The current analysis investigated the 6-month incidence of endoscopically-confirmed peptic ulcer, by baseline CV risk factor(s) (n=2250)
OBERON: peptic ulcer incidence at 6 months, overall population

Values are Kaplan-Meier estimates


RRR, relative risk reduction
OBERON: peptic ulcer incidence at 6 months according to type, overall population

Values are Kaplan-Meier estimates

OBERON: peptic ulcer incidence at 6 months according to ASA dose, overall population

![Bar chart showing the proportion of patients (%) with peptic ulcer incidence at 6 months according to ASA dose, overall population.](image)

- **Esomeprazole 40 mg**
- **Esomeprazole 20 mg**
- **Placebo**

- **Values are observed rates**


ASA, acetylsalicylic acid
## OBERON: baseline CV risk factors

<table>
<thead>
<tr>
<th>Patients with baseline CV risk factors, n (%)*</th>
<th>Esomeprazole 40 mg (n=817)</th>
<th>Esomeprazole 20 mg (n=804)</th>
<th>Placebo (n=805)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>593 (73)</td>
<td>600 (75)</td>
<td>591 (73)</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>362 (44)</td>
<td>335 (42)</td>
<td>339 (42)</td>
</tr>
<tr>
<td>Age &gt;70 y</td>
<td>299 (37)</td>
<td>286 (36)</td>
<td>282 (35)</td>
</tr>
<tr>
<td>Body mass index &gt;30 kg/m²</td>
<td>210 (26)</td>
<td>212 (26)</td>
<td>203 (25)</td>
</tr>
<tr>
<td>Smoker</td>
<td>77 (9)</td>
<td>73 (9)</td>
<td>73 (9)</td>
</tr>
<tr>
<td>History of:**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>111 (14)</td>
<td>116 (14)</td>
<td>101 (13)</td>
</tr>
<tr>
<td>PCI</td>
<td>112 (14)</td>
<td>103 (13)</td>
<td>102 (13)</td>
</tr>
<tr>
<td>CABG</td>
<td>85 (10)</td>
<td>85 (11)</td>
<td>81 (10)</td>
</tr>
<tr>
<td>Stroke</td>
<td>53 (6)</td>
<td>50 (6)</td>
<td>42 (5)</td>
</tr>
</tbody>
</table>

*Patients could have >1 CV risk factor (n=2250; 93% of OBERON study population)

**Not within the previous 3 months

CABG, coronary artery bypass graft; CV, cardiovascular; PCI, percutaneous coronary intervention
OBERON: peptic ulcer incidence at 6 months, by CV risk factor

Proportion of patients (%)

- **Esomeprazole 40 mg**
- **Esomeprazole 20 mg**
- **Placebo**

<table>
<thead>
<tr>
<th>CV Risk Factor</th>
<th>Esomeprazole 40 mg</th>
<th>Esomeprazole 20 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (n=1784)</td>
<td>1.5</td>
<td>1.2</td>
<td>6.8</td>
</tr>
<tr>
<td>Hypercholesterolaemia (n=1036)</td>
<td>1.4</td>
<td>1.2</td>
<td>7.4</td>
</tr>
<tr>
<td>Age &gt;70 y (n=867)</td>
<td>1.3</td>
<td>1.0</td>
<td>5.7</td>
</tr>
<tr>
<td>BMI &gt;30 kg/m² (n=625)</td>
<td>1.9</td>
<td>0.9</td>
<td>6.4</td>
</tr>
<tr>
<td>Smoker (n=223)</td>
<td>0.0</td>
<td>1.4</td>
<td>8.2</td>
</tr>
</tbody>
</table>

Values are observed rates

BMI, body mass index; CV, cardiovascular
OBERON: Peptic ulcer incidence at 6 months, by history of CV events

Values are observed rates

*Not within the previous 3 months

CV, cardiovascular
Conclusions

- Efficacy of esomeprazole in the prevention of peptic ulcer in the investigated CV risk factor subgroups was consistent with the primary analysis.