Statin use and Mortality in Patients with Colorectal Cancer: A Systematic Review and Meta-Analysis of Observational Studies

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Financial Disclosures

• I do not currently have any relevant financial relations to disclose
Off-Label Use Disclosures

I **do intend** to discuss ff-label uses of products during this activity. The following products will be discussed:

• Colorectal cancer mortality and statin use (meta-analysis)
Why

- Statins reduce incidence of CRC
- Pathway- angiogenesis/ proliferation/ apoptosis
- Target population and population at risk takes statins
- Cheap/ easy/ minimal side effects, no need for intervention
Methodology

- Meta-analysis of observational studies evaluating statin use in CRC patients, and its association with overall and CRC-specific mortality.

- Major databases and conference proceedings, through August 2014

- 7 observational studies (64,773 patients with CRC; 19.5% statin users) reporting the association between statin use and mortality in patients with CRC.

- Summary hazard ratio (HR) with 95% confidence intervals (CI) using the random effects model

- Heterogeneity measured using the inconsistency index ($I^2$).
Methodology (contd.)

• Systematic search of Medline, EMBASE, Scopus and Web of Science, up to August 2014 and abstracts from major gastroenterology and oncology conferences (2008-2014).


• Inclusion criteria: (1) clearly defined exposure to statin, (2) reported overall survival or CRC-specific survival in patients with CRC and (3) reported hazard ratio (HR) or provided data for its calculation.

• Random-effects model (DerSimonian and Laird) to calculate summary HR and 95% CI and subgroup analysis using a priori categories

• Heterogeneity assessment: Cochran’s Q statistic, significant for heterogeneity if p value <0.10; and the I² statistic with values >50% being suggestive of significant heterogeneity.
Results

• 7 studies met our inclusion criterion and were included in the analysis, of which 5 studies addressed CRC-specific survival.

• Statin use was associated with a 26% reduction in all-cause mortality in CRC patients as compared to non-use (adjusted HR, 0.74; 95% CI, 0.67-0.83).

• There was minimal heterogeneity between studies in the overall analysis (Cochran's Q test p <0.01, I²=18%).

• On limiting analysis to statin use after diagnosis of CRC, use of statins remained significantly associated with reduced CRC-specific mortality (3 studies; adjusted HR, 0.70; 95% CI, 0.60-0.81), but not overall mortality (4 studies; adjusted HR, 0.82; 95% CI, 0.64-1.05).

• When adjusted for concomitant use of NSAIDs/aspirin, statins were associated with reduced overall mortality (5 studies; adjusted HR, 0.74; 95% CI, 0.66-0.84) and CRC-specific mortality (4 studies; adjusted HR, 0.76; 95% CI, 0.69-0.84).
Association between statin use and overall survival in patients with CRC.
Association between statin use and CRC-specific survival

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log[Hazard Ratio]</th>
<th>SE</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardwell 2014</td>
<td>-0.3425</td>
<td>0.0775</td>
<td>24.6%</td>
<td>0.71 [0.61, 0.83]</td>
</tr>
<tr>
<td>Lakha 2011</td>
<td>-0.6733</td>
<td>0.3638</td>
<td>1.4%</td>
<td>0.51 [0.25, 1.04]</td>
</tr>
<tr>
<td>Ma 2013</td>
<td>-0.3285</td>
<td>0.1016</td>
<td>15.9%</td>
<td>0.72 [0.59, 0.88]</td>
</tr>
<tr>
<td>Mace 2013</td>
<td>-0.478</td>
<td>0.3375</td>
<td>1.7%</td>
<td>0.62 [0.32, 1.20]</td>
</tr>
<tr>
<td>Nielsen 2012</td>
<td>-0.2107</td>
<td>0.0393</td>
<td>56.4%</td>
<td>0.81 [0.75, 0.87]</td>
</tr>
</tbody>
</table>

Total (95% CI) 100.0% 0.76 [0.70, 0.83]

Heterogeneity: $\tau^2 = 0.00; \chi^2 = 4.82, df = 4 (P = 0.31); I^2 = 17\%$
Test for overall effect: $Z = 6.20 (P < 0.00001)$
Conclusions

• Based on meta-analysis of observational studies, statin use in patients with CRC appears to be associated with reduced all-cause mortality and CRC-specific mortality.

• This protective effect seems to be independent of concomitant NSAID/ aspirin use.

• Further prospective investigation of the effect of statins on outcome in CRC patients is warranted.
References

• Ma W, Shao YY, Hsu C et al. *J Clin Oncol* 31, 2013 (suppl; abstr 3554)
• Thank you

• Questions/ comments

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