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

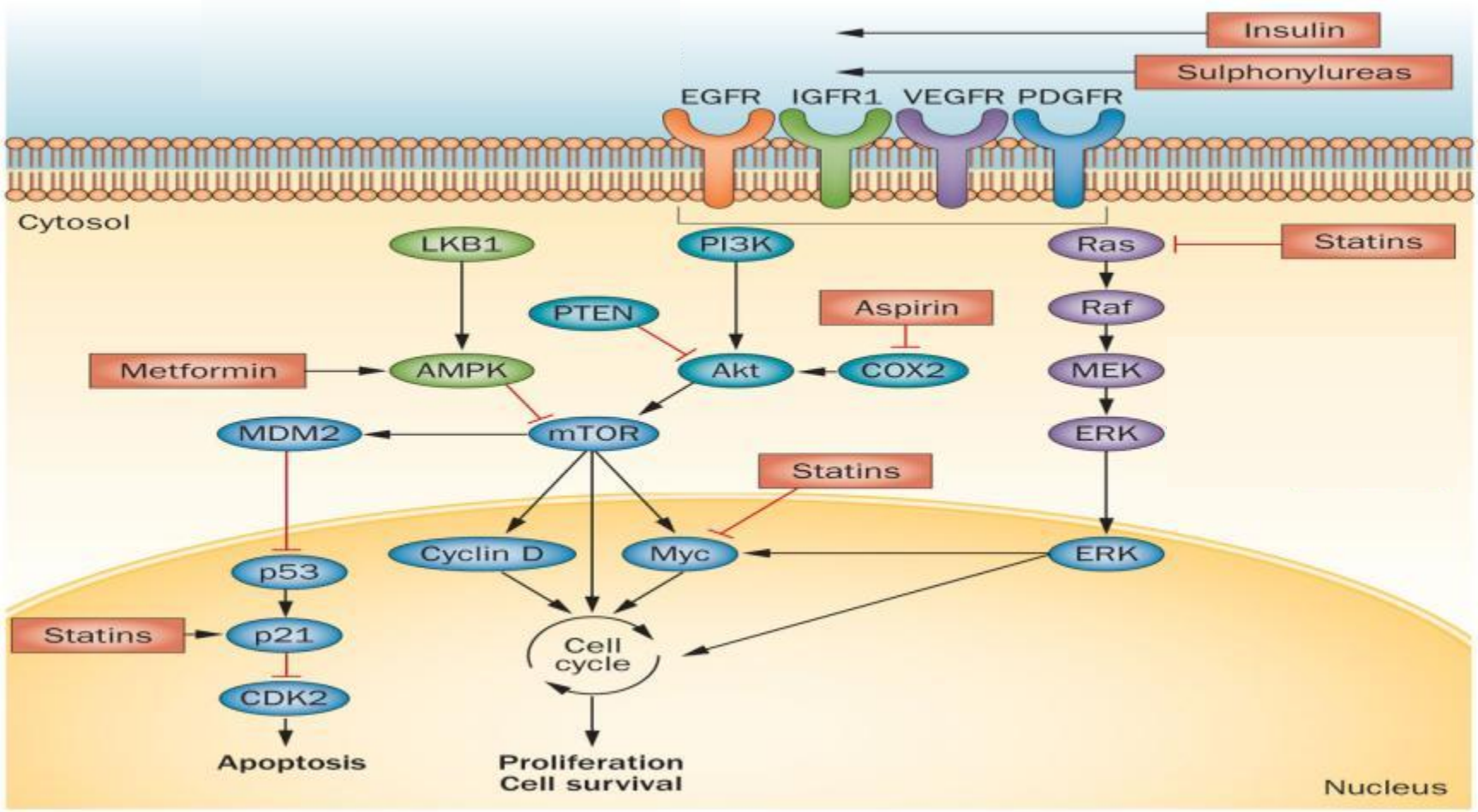
I **do intend** to discuss ff-label uses of products during this activity. The following products will be discussed:

- 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

Metabolic Pathway



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).
- Keywords and medical subject heading terms used: ‘statin’, ‘HMG-CoA reductase inhibitor’, ‘survival’, ‘mortality’, AND ‘colon cancer’ OR ‘colon’, ‘rectal’ AND ‘neoplasia’, ‘colorectal adenocarcinoma’
- 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 I^2 statistic with values >50% being suggestive of significant heterogeneity.

Results

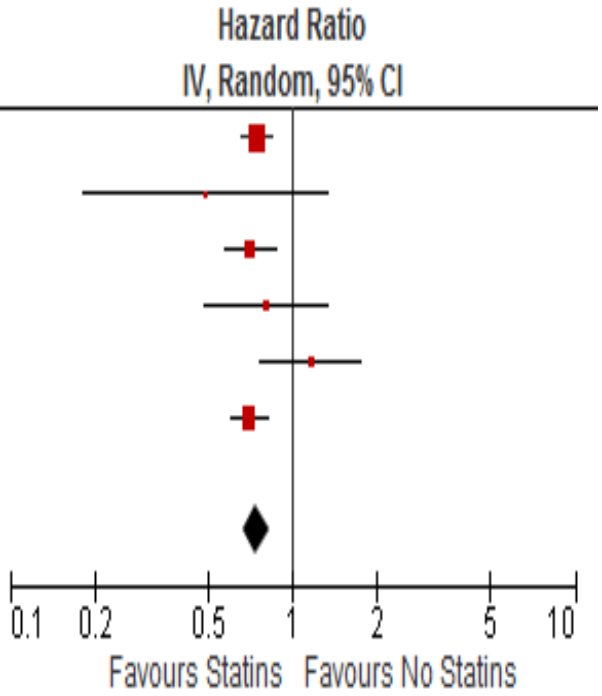
- 7 studies met our inclusion criterion and were included in the analysis, of which 5 studies addressed CRC-specific survival.
- Statin use was associated with a 26% reduction in all-cause mortality in CRC patients as compared to non-use (adjusted HR, 0.74; 95% CI, 0.67-0.83).
- There was minimal heterogeneity between studies in the overall analysis (Cochran's Q test $p < 0.01$, $I^2 = 18\%$).
- 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.

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
Cardwell 2014	-0.2877	0.0652	38.3%	0.75 [0.66, 0.85]
Lakha 2011	-0.7133	0.511	1.1%	0.49 [0.18, 1.33]
Ma 2013	-0.3425	0.1032	20.4%	0.71 [0.58, 0.87]
Mace 2013	-0.2107	0.2564	4.1%	0.81 [0.49, 1.34]
Ng 2011	0.1484	0.2091	6.0%	1.16 [0.77, 1.75]
Siddiqui 2009	-0.3567	0.0786	30.3%	0.70 [0.60, 0.82]
Total (95% CI)			**100.0%**	**0.74 [0.67, 0.83]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.10$, df = 5 (P = 0.30); $I^2 = 18\%$

Test for overall effect: Z = 5.59 (P < 0.00001)

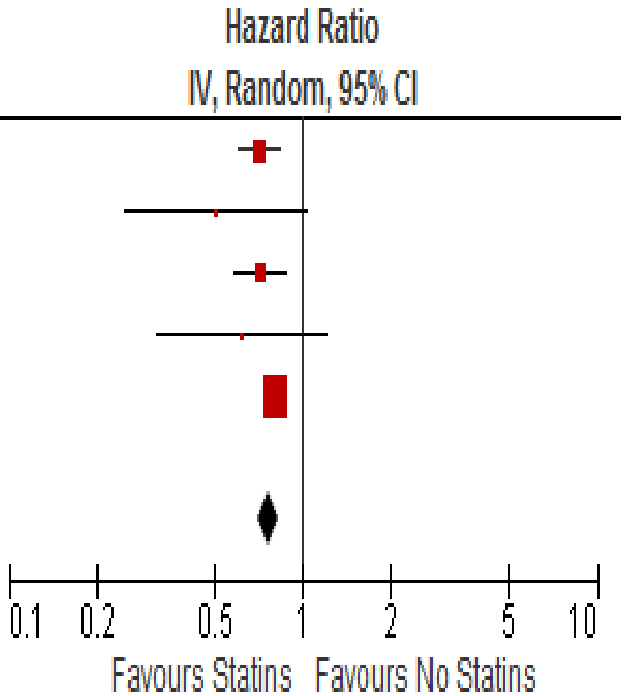


Association between statin use and CRC-specific survival

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

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- Thank you
- Questions/ comments
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