Clinical Studies of Aspirin and Cancer Prevention Signals

NCI Board of Scientific Advisors
National Cancer Advisory Board

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Caveats

- Will only present the potential benefits
  - Not harms

- Most benefits are expressed as relative rates
  - Not in terms of absolute rate reduction

- The evidence presented is insufficient to make public policy or guidelines

- The U.S. Preventive Services Task Force is currently performing a systematic review of benefits and harms for cancer prevention
Daily Aspirin (≥ 5 yrs) Use and Colorectal Cancer Risk

- Randomized trials: Relative Risk = 0.55, p=0.0005
- Case control: Relative Risk = 0.63, p=0.004
- Standard cohort: Relative Risk = 0.68, p=0.006
- Nested case-control: Relative Risk = 0.51, p=0.012

Aspirin Use and Risk of Cancer
(maximum reported use of aspirin)

Case-control studies (odds-ratio)

Cohort studies (risk ratio)

Randomized Trial Data
- Significant effect (p<0.05)
- Non-significant effect (p>0.1)
- Trend (p<0.1)

Algra & Rothwell.
Effect of Low-dose (75-300mg) Aspirin Vs Control on Colorectal Cancer Incidence & Mortality

- Incidence
- Mortality

Data from 4 randomized trials of aspirin vs. control

Rothwell, Lancet, 20 November 2010
Aspirin Use and Cancer Metastasis

**Lung metastasis**

- Aspirin: HR 0.34 (95% CI 0.14–0.83), p=0.018
- Control

**Liver metastasis**

- Aspirin: HR 0.66 (95% CI 0.42–1.03), p=0.07
- Control

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<th>Control</th>
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Rothwell et al., Lancet 2012; 379: 1591–601
Daily Aspirin Use and Cancer Metastasis: (5 RCTs)

Aspirin at initial diagnosis (any metastasis)

- All solid cancers: Hazard Ratio 0.73, p=0.002
- Adenocarcinoma: Hazard Ratio 0.60, p=0.0001
- Non-adenocarcinoma: Hazard Ratio 0.96, p=0.81
- Colorectal cancer: Hazard Ratio 0.26, p=0.0008

Aspirin at initial diagnosis and remained on Aspirin

- Adenocarcinoma: Hazard Ratio 0.31, p=0.0009

Rothwell et al., Lancet 2012; 379: 1591–601
Aspirin (≥ 20 yrs) on Death Due to Cancer
(pooled 2° analysis from 3 RCT, n=10,502)

Rothwell et al., Lancet 2011; 377: 31-41
Key Points: Aspirin for Cancer Prevention

• Regular aspirin use is associated with reduction in the long-term risk of developing a variety of cancers [cohort, case-control & randomized clinical trials]

• Evidence strongest for GI cancers

• May reduce metastasis in patients taking aspirin prior to diagnosis of cancer [randomized trials]

• Need mechanistic studies of aspirin effects across the spectrum of pathogenesis, progression, and metastasis
Extra Slides
Maximum Opportunity to Interrupt Cancer Progression

Cancer Progression

- Normal
- Precancer
- Carcinoma \textit{in situ}
- Cancer
- Metastasis
- Cancer Mortality

Cancer Treatment

Cancer Prevention

Survival without Cancer
Survival with Cancer

Umar et al., Nature Reviews Cancer 12, 835-848