

Chemoprevention of Esophageal Cancer with esomeprazole and aspirin therapy: efficacy and safety in the phase III randomized factorial AspECT Trial

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Abstract

Background

Esophageal adenocarcinoma (EA) is the sixth most common cause of global cancer death. We rely on endoscopy screening to identify and monitor patients with Barrett's esophagus (BE) and find neoplastic lesions early enough to manage their EA. This approach has a modest effect on EA supported by low quality evidence. We evaluated the efficacy of aspirin and high dose acid suppression in preventing EA in patients with BE.

Methods

We recruited patients with ≥ 1 cm of BE and no high grade dysplasia (HGD) or EA at baseline in UK and Canadian hospitals. To conceal allocation, a central trials unit randomized patients using a computer-generated schedule. Patients were randomized unblinded 1:1:1:1 in a 2X2 factorial design to high dose (40mg twice daily) or low dose (20mg once daily)esomeprazole proton pump inhibitor acid suppression (PPI) , alone or combined with low dose aspirin 300mg/day (330mg in Canada). The primary composite endpoint was time to all-cause mortality or EA or HGD analyzed using accelerated failure time modelling adjusting for minimization factors (age, length of Barrett's esophagus and presence of intestinal metaplasia).

Results

We recruited 2563 Barrett's patients followed-up for a median of 8.9 years (interquartile range 8.2-9.8) with 20,095 years of follow up. There were 313 events of the composite primary endpoint. High dose PPI was statistically significantly superior to low dose PPI ($p=0.037$, $N=2535$, Time Ratio (TR) 1.27, 95% CI = 1.01-1.58). Aspirin therapy showed a trend to benefit but was not statistically significant ($p=0.068$, $N=2280$, $TR=1.24$, 95% CI = 0.98 – 1.57). The combination of aspirin with high dose PPI had the strongest effect compared to low dose PPI with no aspirin ($TR = 1.59$, 95% CI = 1.14 to 2.23, $p=0.007$). There were few serious adverse events reported (1.0% of patients), with 99.9% data collected.

Conclusions

This is the largest randomized controlled chemoprevention trial in patients with Barrett's esophagus. We have shown that PPI high dose and aspirin chemoprevention therapy, especially in combination significantly reduces rates of death, EA or HGD occurrence and is safe.

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