

Independent analyses of the cancer rates in the SEAS, SHARP and IMPROVE-IT studies of ezetimibe

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Summary

The two hypothesis-testing trials (SHARP and IMPROVE-IT) contain about four times as many cancers as the SEAS trial.

They do not confirm the hypothesis raised by the SEAS trial that treatment increases the overall risk of developing cancer.

As there is no increase with time in the relative risk (active vs placebo) suggested by the cancer incidence and mortality from all 3 trials together (or just from the pair of hypothesis-testing trials), the SEAS, SHARP and IMPROVE-IT trials do not provide credible evidence of any adverse effect on cancer.

Background: Results from 90,000 patients in 14 statin trials: safety of cholesterol-lowering and safety of statins

Allocation to 5 years of substantial LDL-cholesterol lowering by a statin has no apparent effect on cancer. The Cholesterol Treatment Trialists' collaboration (CTT, Lancet 2005; 366: 1267-78) includes 90,000 patients randomised evenly between statin (which substantially lowers LDL-cholesterol) and control.

Based on 5530 patients with cancer onset after randomisation, the statin vs control relative risk was 0.997 (with 95% confidence interval 0.95-1.05; not significant).

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Of these patients, 2163 died of their cancer during the scheduled follow-up period; the relative risk for cancer death was 1.01 (with 95% confidence interval 0.91-1.12; not significant).

NB: Within this null average, some trials suggested a decrease and some an increase in overall cancer or in particular types of cancer, but no type of cancer was clearly increased or decreased in the aggregated data from all 14 trials. An independent meta-analysis of these results was previously provided to regulatory authorities in Europe by the CTSU.

MAIN RESULT: No overall increase in the total number of patients with cancer in the two hypothesis-testing trials

	Active	Control
Hypothesis generator; SEAS trial (~2000 pts)	102	67
Hypothesis test: SHARP & IMPROVE-IT trials (~20,000 pts)	313	326

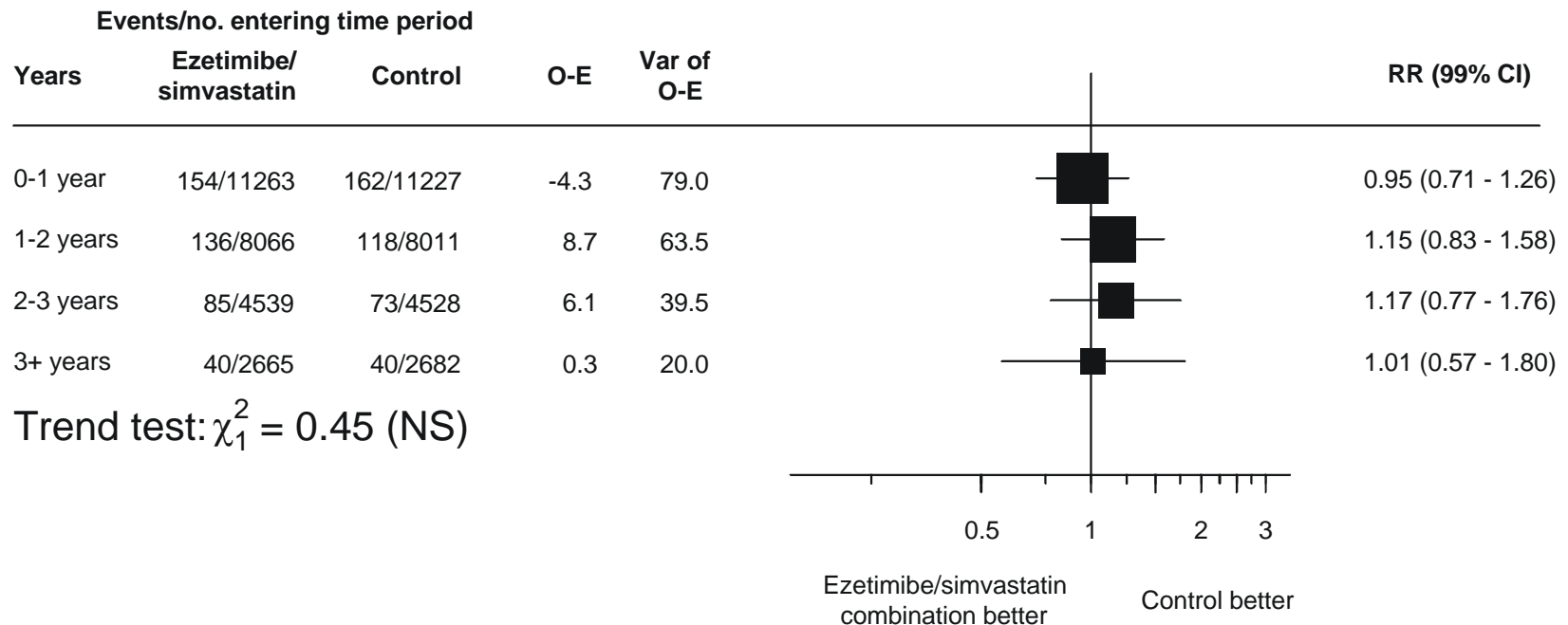
Cancer incidence in the IMPROVE-IT and SHARP trials

	Active	Control
Number randomized	10,319	10,298
Digestive tract	57	61
Hepatobiliary/pancreatic	15	18
Respiratory/intrathoracic	37	30
Skin	74	89
Breast	21	19
Prostate	25	36
Kidney	25	11
Bladder	19	20
Genital	6	5
Haematological	18	19
Other known sites	13	12
Multiple/unspecified	28	19
Total: Any cancer	313	326

If active treatment causes a real increase in cancer incidence, then the relative risk for cancer (active vs. placebo) should get significantly bigger with time, but it does not.

Ratio, active vs. control, of cancer incidence rates in the 1st, 2nd, 3rd, and subsequent years separately: All 3 trials together (SEAS, SHARP, & IMPROVE-IT)

CANCER INCIDENCE RATE RATIO (RR; ANY SITE, 10th ICD C00-C99)



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(Likewise, nor does the relative risk for cancer mortality increase with time)

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