of Tregs in many solid tumors correlate inversely with patient survival.[5] Moreover, the elderly have depressed immune functions[6] and are more likely than younger subjects to harbor microscopic foci of cancer cells. Therefore, further impairment of immune function in the elderly likely increases the chance of occult tumor growth.

Importantly, statin trials have largely excluded subjects with prevalent or remote cancer. In practice, elderly patients are treated with statins regardless of cancer status. It is quite possible that in the routine treatment of elderly subjects with statins, an increase cancer incidence and mortality may exceed in magnitude any decrease in cardiovascular disease morbidity and mortality. Perhaps suboptimal use of statin therapy in the elderly is actually a blessing in disguise.

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REFERENCES

1. Al-Omran M, Mamdani MM, Lindsay TF, Melo M, Juurlink DN, Verma S, Systemic Assessment of Vascular Risk Investigators. Suboptimal use of statin therapy in elderly patients with atherosclerosis: a population-based study. J Vasc Surg 2008;48:607-12.
2. Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet 2002;360: 1623-30.
3. Mausner-Fainberg K, Luboshits G, Mor A, Maysel-Auslender S, Rubinstein A, Keren G, George J. The effect of HMG-CoA reductase inhibitors on naturally occurring $CD4^+CD25^+$ T cells. Atherosclerosis 2008;197: 829-39.
4. Goronzy JJ, Weyand CM. Immunosuppression in atherosclerosis: mobilizing the opposition within. Circulation 2006;114:1901-4.
5. Yakirevich E, Resnick MB. Regulatory T lymphocytes: pivotal components of the host antitumor response. J Clin Oncol 2007;25:2506-8.
6. Gruver AL, Hudson LL, Sempowski GD. Immunosenescence of ageing. J Pathol 2007;211:144-56.

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Reply

In response to the letter to the editor by Dr Mark R. Goldstein, et al, entitled "Might suboptimal use of statin therapy in the elderly be a blessing in disguise?," the authors pointed out that suboptimal use of statin might do more harm than good in the elderly because of the increased risk of cancer in these patients. However, the association between statin use and the development and/or prevention of cancer has been conflicting.

Although at the experimental level, statins have been demonstrated to contribute to the development of cancer by acting as immunoregulators, other studies have shown that statins could trigger cells of certain tumor types to undergo apoptosis,[1] which may be the basis for the inhibitory effect of statins on cancer cell proliferation.[2]

In 2002, the PROspective Study of Pravastatin in the Elderly at Risk (PROSPER) suggested an increased incidence of cancer diagnosed during the treatment period of 3.2 years (245 [8.5%] in pravastatin group vs 199 [6.8%] placebo group, $P = .02$).[3] However, these findings have not been replicated consistently in subsequent large clinical trials and thus may be attributable to chance findings. Indeed the Heart Protection Study, the largest clinical trial to study the benefits of statins in over 20,000 high-risk individuals, conclusively demonstrated their benefits among a broad population, including the elderly, without an increased risk for cancer.[4]

Further, other studies have suggested a large protective effect of statins on certain cancers in the elderly population. A large population-based study compared 25,594 non-statin users' patients to 37,248 patients using statins showed that statin users had a statistically significant lower risk for total cancer than nonusers after adjustment for age (hazard ratio [HR] = 0.76, 95% confidence interval [CI] = 0.73 to 0.80) and multiple potential confounders (HR = 0.74, 95% CI = 0.70 to 0.78).[5]

Other studies have suggested a neutral effect of statins on cancers. A recently published meta-analysis of 20 trials studied patients treated with statins found that statins have a neutral effect on cancer and cancer death risks (odds ratio [OR], 1.02; 95% CI, 0.97-1.07) and (OR, 1.01; 95% CI, 0.93-1.09), respectively.[6]

In conclusion, the currently available evidence consistently demonstrates significant cardiovascular benefit for statins without significant harm. An association between statins and cancer has not been firmly established and cannot be based on the findings of a single trial. Without conclusive evidence from additional observational studies and randomized trials that examine the association between statins and cancer (causation, prevention, or neutral effect), statin use for the primary and secondary prevention of cardiovascular adverse events should be continued in the elderly patients in a similar way as in the younger population.

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REFERENCES

1. Wong WW, Dimitroulakos J, Minden MD, Penn LZ. HMG-CoA reductase inhibitors and the malignant cell: the statin family of drugs as triggers of tumor-specific apoptosis. Leukemia 2002;16:508-19.
2. Kusama T, Mukai M, Iwasaki T, Tatsuta M, Matsumoto Y, Akedo H, et al. 3-hydroxy-3-methylglutaryl-coenzyme a reductase inhibitors reduce human pancreatic cancer cell invasion and metastasis. Gastroenterology 2002;122:308-17.
3. Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet 2002;360: 1623-30.
4. Heart Protection Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002;360:7-22.
5. Farwell WR, Scranton RE, Lawler EV, Lew RA, Brophy MT, Fiore LD, Gaziano JM. The association between statins and cancer incidence in a veterans population. J Natl Cancer Inst 2008;100:134-9.
6. Dale KM, Coleman CI, Henyan NN, Kluger J, White CM. Statins and cancer risk: a meta-analysis. JAMA 2006;295:74-80.

doi:10.1016/j.jvs.2008.12.050