

Questions and Answers About Beta Carotene Chemoprevention Trials

1. What is a chemoprevention trial?

A chemoprevention trial is a type of clinical trial, which is a research study conducted with people. In a cancer chemoprevention trial, natural or laboratory-made substances are tested to see if they prevent cancer. The people who participate in such a study are healthy or are at risk of developing cancer, or in some studies, people who have been diagnosed with cancer and are at risk of developing a second cancer.

2. What is the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Trial?

The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Trial or ATBC Trial was conducted by the National Cancer Institute (NCI) in collaboration with the National Public Health Institute of Finland. The purpose of the study was to see if certain vitamin supplements would prevent lung and other cancers in a group of 29,133 male smokers in Finland. The 50- to 69-year-old participants took a pill containing either 50 milligrams (mg) alpha tocopherol (a form of vitamin E), 20 mg beta carotene (a precursor of vitamin A), both, or a placebo (inactive pill that looks like the vitamin) daily for five to eight years.

3. What is the Beta Carotene and Retinol Efficacy Trial or CARET?

The Beta Carotene and Retinol Efficacy Trial or CARET is a large NCI-funded chemoprevention trial that is being conducted in six areas in the United States. The purpose of the study was to see if the combination of beta carotene and vitamin A (a retinol) supplements would prevent lung and other cancers in men and women ages 50 to 69 who are smokers or former smokers, and men ages 45 to 69 who have been exposed to asbestos. The 18,314 participants stopped taking the supplements prior to the completion of the trial.

4. What is the Physicians' Health Study?

The Physicians' Health Study is a chemoprevention trial with 22,071 U.S. male physicians, of which only 11 percent smoked. The purpose of the study was to test whether a beta carotene supplement reduced the risk of cancer and heart disease as well as whether low-dose aspirin reduced the risk of heart disease. The aspirin component



was stopped in early 1988 due to a 44 percent reduction in risk of first heart attack among those taking aspirin. The beta carotene component ended December 31, 1995, after more than 12 years of study.

5. What did these trials show?

In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Trial, 18 percent more lung cancers were diagnosed and 8 percent more overall deaths occurred in study participants taking beta carotene. In CARET, after an average of four years of receiving supplements, 28 percent more lung cancers were diagnosed and 17 percent more deaths occurred in participants taking beta carotene and vitamin A than in those taking placebos. Neither of these studies showed a benefit from taking supplements.

Because the interim results of CARET were similar to the ATBC study, the intervention was stopped 21 months early. Both of these studies involved people who were specifically invited to participate because of their high risk for developing lung cancer.

The Physician's Health Study was completed at the end of 1995 and showed no benefit or harm in people taking beta carotene supplements for more than 12 years.

6. Why did CARET stop early?

The study itself was not stopped, but the participants were told to stop taking the beta carotene and vitamin A or placebos. The Safety and Endpoints Monitoring Committee for CARET and an ad hoc committee assembled by NCI saw that the interim results clearly showed no benefit from the supplements and also showed there was a possibility that they were harming participants. CARET investigators made the decision to stop the intervention, but they will follow the study group for five more years to determine the long-term effects of the intervention.

The intervention was halted on January 11, 1996, by the CARET investigators. Letters were mailed to participants by January 13 and a public announcement made on January 18.

7. Who were the participants in CARET?

The study had two groups: 14,254 current and former smokers with a long history of smoking, and 4,060 asbestos-exposed individuals.

The smokers and former smokers included 14,254 men and women ages 50 to 69 who were current smokers or were smokers who had quit within six years of enrolling in the study. Smokers and former smokers must have had a smoking history of at least 20 pack years (one pack per day for 20 years or two packs for 10 years, etc.). These participants were 56 percent male (7,965) and 44 percent female (6,289), and had an average of 50 pack years of smoking. About 34 percent were former smokers when they joined the study. All participants were counseled to quit smoking at their visits to the study centers.

The asbestos-exposed participants were 4,060 men ages 45 to 69 who had been exposed to asbestos while at work. These participants had to have extensive occupational asbestos exposure beginning at least 15 years prior to enrollment, determined by either a chest X-ray that showed asbestos exposure, or employment for more than five years in trades that carry a high risk of exposure to asbestos (plumbers and pipe fitters, steam fitters, shipyard boilermakers, non-shipyard boilermakers, shipyard electricians, shipscalers, insulators, plasterboard workers, or sheet metal workers). In addition, they had to be either current smokers or had to have quit smoking within the last 15 years.

8. What is beta carotene?

Beta carotene, which is found in plants, is a precursor of vitamin A. The body converts beta carotene to vitamin A. It occurs mainly in fruits and vegetables that are deep yellow, orange, or dark green in color, such as carrots, squash, yams, peaches, apricots, spinach, collard or mustard greens, and broccoli. It is an antioxidant, a compound that may prevent cancer-causing substances from damaging DNA. Epidemiologic studies have linked high intake of foods rich in beta carotene and high serum levels of the micronutrient to a reduced risk of cancer, particularly lung cancer.

9. What is vitamin A?

Vitamin A is a vitamin, a substance found in foods that is necessary for human health. Vitamin A is found in liver, various dairy products with fat, such as milk, cheese, butter and ice cream, and in fatty fish such as herring, sardines, and tuna. It can also be found in the liver oils of shark, cod, and halibut. Vitamin A is known to play a part in cell differentiation, a process by which cells “mature.” Differentiation helps prevent inappropriate growth, such as the uncontrolled cell growth that is seen in cancer. Many studies in animals show that vitamin A and similar compounds decrease the incidence of cancer.

10. Should Americans who smoke avoid taking beta carotene?

The NCI has never made recommendations as to whether Americans should take supplements. The best advice for smokers who want to reduce their risk of lung cancer is still the most direct: stop smoking. The results from CARET and the ATBC Trial suggest that smokers should avoid taking beta carotene supplements.

11. Should Americans who don't smoke take beta carotene supplements?

The results of the Physicians' Health Study showed no benefit or harm to nonsmokers who took beta carotene every other day for 12 years. The results from CARET and the ATBC Study do not provide information about the effects of beta carotene supplements on non-smokers.

NCI does not make recommendations as to whether Americans should take supplements. For those who wish to reduce their risk of cancer, NCI advises that it is prudent to adopt a low-fat diet containing plenty of fruits, vegetables, and grains.

12. Should Americans stop eating five fruits and vegetables daily (5-A-Day)?

No. 5-A-Day remains a good idea. In both the ATBC Study and CARET, participants with the highest levels of beta carotene in their blood, measured before the study began, went on to have fewer lung cancers. These results are consistent with the possibility that a different compound or compounds in foods that have high levels of beta carotene may be responsible for the protective effect of dietary beta carotene seen in epidemiologic studies. Because these are studies of pills, not food intake, NCI stresses that the study results do not change the results of studies that show that eating a variety of fruits and vegetables each day remains a good way to reduce the risk of some cancers.

13. What other chemoprevention studies are under way with beta carotene?

The NCI has a number of different agents under study, including calcium, fiber, tamoxifen, and others. Only one large-scale study including beta carotene (the Women's Health Study) was ongoing when CARET stopped its intervention, and the beta carotene portion of that study has been halted. Principal investigators of smaller or shorter-term studies including beta carotene were alerted and advised to consider the results of these studies in making decisions about the studies they are conducting.

In the Women's Health Study, sponsored by the National Institutes of Health, 40,000 apparently healthy women health professionals ages 45 and older were being assigned at random to 50 mg beta carotene, 600 IU vitamin E, 100 mg aspirin, and/or placebos every other day. The beta carotene portion of this trial was dropped. The trial, which began in 1992, will show the balance of benefits and risks of these agents on cancer and cardiovascular disease.

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1-800-4-CANCER (1-800-422-6237)

TTY (for deaf and hard of hearing callers): 1-800-332-8615

NCI Online

Internet

Use <http://cancer.gov> to reach the NCI's Web site.

LiveHelp

Cancer Information Specialists offer online assistance through the *LiveHelp* link on the NCI's Web site.

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