

May 2018

SELECT: Selenium and Vitamin E Cancer Prevention Trial

Summary:

SELECT is a phase III randomized, placebo-controlled trial of selenium (200 ug/day from *L*-selenomethionine) and/or vitamin E (400 IU/day of *all rac*- α -tocopheryl acetate) supplementation (planned minimum of 7 years and maximum of 12 years) for prostate cancer prevention. The major eligibility requirements included age of ≥ 50 years for African American men and ≥ 55 years for all other men, no prior prostate-cancer diagnosis, PSA ≤ 4 ng/mL, and a DRE not suspicious for cancer. No current use of anticoagulant, no history of hemorrhagic stroke, and normal blood pressure were also required because of anti-platelet effects of vitamin E and related findings of the ATBC.

A total of 35,533 men, 1800 who had previously been on PCPT, were accrued and randomly assigned at 427 participating sites in the United States, Canada and Puerto Rico between August 22, 2001, and June 24, 2004, achieving minority representation of 21% (15% African Americans). A variety of recruitment methods were used with an emphasis on minority recruitment. Study supplementation ended in 2008 and the results were reported early due to convincing evidence (planned futility analysis) that neither vitamin E nor selenium supplements were associated with prevention of prostate cancer (Lippman SM, Klein EA, Goodman PG, et al: JAMA 2009; 301:39-51). In an updated analysis in 2011, with a median follow-up of seven years, the supplemental vitamin E arm showed a statistically significant increased risk of prostate cancer compared to placebo (hazard ratio 1.17, 99% confidence interval 1.00, 1.36) (Klein EA, Thompson IM, Tangen CT, et al: JAMA 2011; 306:1549-1556). The public health impact of such a finding is far-reaching and prompts many questions.

Data collection:

Participants had clinic visits once every 6 months throughout the trial: adherence and adverse events were monitored every 6 months, and a limited physical examination including assessments of blood pressure, weight and smoking status was conducted annually. An extensive assessment of dietary supplement use was also collected at baseline and supplement use was updated annually. Annual prostate cancer screening with PSA and DRE was not mandatory since the benefits of this screening were under debate when the trial opened and community screening standards were expected to change during the trial. Participants were recommended during annual clinic visits to undergo a PSA test and DRE according to the standard of care at their study sites and the participant's wishes. Prostate cancer detection was thus based on community standards and confirmed by central pathology review. Prostate tissue samples were stored for future research. Adherence measures included pill counts on all and plasma levels of alpha- and gamma-tocopherol and selenium in all participants at a subset of study sites (7.8% of the trial population).

Baseline data included the following:

- Medical history
 - Disease: Cancer, cardiac, diabetes, chronic lung disease, cataract, macular degeneration
 - Prostate: BPH, prostatitis, procedures; finasteride, testosterone, anabolic steroid use
 - Medication use: Aspirin, Cox II inhibitors, NSAIDs, statins
- Family history of cancer
 - Prostate, colorectal, lung cancers
- Food Frequency Questionnaire
 - Foods and supplements
- Participant characteristics
 - Age, race, PSA
 - Smoking status
 - Education, living arrangement

Post baseline data:

Men were asked at their first 6-month clinic visit to report new events since entering the trial and thereafter to report new events since their last visit. Cardiac event data were collected in detail from the trial beginning (2001); data on diabetes were added through self-reported glitazone-medication use (beginning in 2003) and diagnosis of diabetes (beginning in late 2005).

Prostate cancer and health were monitored via the annual DRE and PSA monitoring as well as a recording of all prostate procedures, BPH, PIN, prostatitis. Colorectal screening procedures were collected every six months as were questions regarding ocular and lung health.

Side effect monitoring included recording of the incidence of pre-specified toxicities known to be associated with the study supplements (nausea, fatigue, nail changes, halitosis, alopecia, dermatitis), cardiac events and procedures, self-report of diabetes and any grade 3 or 4 events regardless of attribution to study supplements.

Other post-baseline covariate data collected included an annual update on medication usage (expanded list) as well as supplement use (vitamins C, E, D, selenium, zinc, calcium, folic acid, lycopene, beta-carotene).

CFU: Centralized Follow-Up

After the active intervention on SELECT, participants were followed by their local study sites for approximately one year. After that, the study transitioned to a Centralized Follow-Up (CFU) where the participant follow-up contact was to be done by the Statistical Center and initially conducted primarily by mail.

Data collection during CFU was kept to a minimum and focused on study endpoints and the participant's general health, along with the participant's contact information. The general approach to question structure was to use closed-ended questions with check boxes and minimize the amount of text and numeric answers. The questions were worded to be understandable to the population and examples were provided when applicable. For example, the questions about prostate cancer treatments used the scientific name(s) as well as the commonly used name. Shading is used for multiple part questions to guide the eye.

Transition to Centralized Follow-Up (CFU) began Nov, 2009. A total of 17,780 participants (15% minority, 11% African American), 1100 of whom were also on the Prostate Cancer Prevention Trial (PCPT), transitioned to the CFU. The CFU allowed us to monitor the incidence of new prostate and other cancers, to evaluate whether the increased risk of prostate cancer in the vitamin E arm is maintained or disappears with time, and to evaluate any long-term effects associated with these cancers. It also gave us the opportunity to contact participants regarding other cancers, and to potentially obtain permission to gain access to their prostate cancer tissue when applicable. We also collected data about treatment of prostate cancer and PSA values. Funding for this phase of SELECT ended and the CFU concluded in May 2014.