

Prospective multicenter ovarian cancer screening trial of women at high risk: Preliminary results from the first 2,200 women.

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Objectives. Women with a BRCA mutation have a 20 to 40 percent lifetime risk of ovarian cancer.¹ The current recommendation for such women for reducing the risk of ovarian cancer is prophylactic oophorectomy.² Nonetheless, some high-risk women choose to retain their ovaries, even though no proven screening strategies exist for this high-risk group.^{3 4} Other women at elevated risk include subjects from families with multiple ovarian or breast cancers. A multicenter prospective ovarian cancer screening study of women at high risk examined a strategy with CA125 as first-line test, followed by transvaginal sonography (TVS). This report summarizes the performance of the trial to date and examines the effect of demographic and other factors on baseline CA125 to establish normal cutpoints (CPs) within subgroups for referral to TVS, which is crucial for maintaining high specificity in a first-line ovarian cancer screening test.

Methods. Twenty-three US academic medical centers are participating in this trial. High-risk eligibility criteria included the proband or 1st- or 2nd-degree relatives (DRs) with either a BRCA mutation or multiple breast or ovarian cancers or Ashkenazi heritage and at least one 1st DR or two 2nd DRs with breast or ovarian cancer. Subjects with previous ovarian cancer were excluded. The 98th percentile is used as a CP to ensure that 98 percent first-line specificity is maintained. ANOVA was used to assess whether CA125 means differed statistically between subgroups.

Results. The study has enrolled 2,200 eligible subjects to date, which is 5 percent ahead of expected [accrual rates]. A total of 34 subjects (1.7 percent) subsequently withdrew consent or were lost to follow-up. Compliance with the protocol of three monthly blood draws was excellent, with 84 percent, 83 percent, 85 percent, and 87 percent of subjects with previous draw returning within a 1-month window of target date for the 2nd, 3rd, 4th, and 5th draws, respectively. Factors that changed the CP >10 percent and defined >3 percent of the population were menopausal status, race, smoking, and bilateral salpingo-oophorectomy (BSO). The CP [for] postmenopausal women (n=995) is 34U/mL, while for premenopausal subjects (n=933) CP increases to 53U/mL (p<.01). *Premenopausal women:* African Americans (n=35) have a lower CP of 39U/mL (p<.01). Smoking decreases the CP to 44U/mL (p=.02). *Postmenopausal women:* BSO substantially reduced CP to 28U/mL.

Conclusions. Accrual has exceeded expectations and compliance with three monthly blood draws is excellent. For future studies, menopausal status, smoking status, and race should be utilized in defining CPs for appropriate referral to TVS among subgroups. The standard cutpoint of 35 U/mL is appropriate for referral to TVS among postmenopausal women at high risk for ovarian cancer. For African-American premenopausal women, the cutpoint should be around 40 U/mL. For other premenopausal women at high risk, a cutpoint of 50 U/mL is appropriate, with a lower cutpoint of 45 U/mL for current smokers.

References

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