

What is OncoVue?

OncoVue is a genetic test being offered by Opaldia. The following quotes are from the Opaldia website.

“OncoVue helps a woman know her risk of developing breast cancer compared with the average female population between the ages of 35-65.”

“OncoVue was developed based on a large and study of women who were diagnosed with breast cancer and women who have never been diagnosed with any form of cancer. The study, performed by InterGenetics, included over 9000 women. Of these, 3100 had breast cancer and 5900 were cancer free. In addition to looking at variations in genes influencing the average woman’s breast cancer risk, some personal medical and family history measures from the United States of America’s National Cancer Institute’s Breast Cancer Risk Assessment Tool, as well as others indicated in InterGenetics studies and other published studies were included.”

“The OncoVue analysis examines 117 common genetic variations in over 100 genes. The test is based on the examination of a subset of these genetic variations plus the personal medical and family history variables.”

The technical details provided on the website do not list the 117 common variants that are being included in this test. The study by InterGenetics referred to was published recently ¹ and is reviewed in brief below.

The Intergenetics Study

Analysed 18 SNP in 12 genes in steroid hormone metabolism and signalling pathways. Two case-control studies were available for analysis. The first was analysed for all SNPs and the second was only tested for SNPs with a nominally significant ($P < 0.05$) result in the first study.

Study 1: 1667 BC cases and 3333 controls

Study 2: 526 BC cases and 1057 controls

Genotyping used an allele specific primer extension assay. Basic quality assurance of genotyping data were good. Statistical methods used were standard using a chisquared test to compare genotype frequencies in cases and controls. Data were analysed for a main effect and in three age specific sub-groups.

In the main effects analysis there was one significant association (*SOD2* V16A) in first set but not replicated in second set. This variant has been studied by numerous other groups and a meta-analysis of these data showed no significant association².

Age specific sub-group analyses were carried out for age groups 30-44, 45-54 and 55-59. Significant associations in one or more age groups at a nominal $P < 0.05$ were found for 5 SNPs. None were independently validated in second set at same level of significance, but direction of effect was same for 4 of the SNPs (there is a 20% probability of this occurring by chance if none are truly associated). These were described as confirmed associations! No combined data analyses were reported.

Limited discussion of results from other studies that have investigated the same genes/SNPs.

Comment

No combined data analyses reported.

“Validated” age specific effects for *PGR* V660L and *CYP19* 3’UTR have little biological plausibility as risks confined to those aged 45-54 and not present in younger or older women. The UGT1A7 K131R effects with increased risk in younger women and decreased risk in older women also unlikely from biological perspective.

Conclusion

Evidence for majority of SNPs used in OncoVue not possible to assess as it is not known what SNPs are. Given low prior odds for any of the SNPs assessed by Ralph et al, most reported associations at the $P < 0.05$ level will be false positive (see ³ and ⁴ for explanation). Even where strong prior based on candidate genes, $P < 10^{-6}$ probably reasonable threshold. Prior odds for age specific effects with unusual distributions are even smaller and even more stringent P-value thresholds would be appropriate.

Risk assessemtn based on OncoVue very unlikely to be reliable or valid.

References

1. Ralph DA, Zhao LP, Aston CE, Manjeshwar S, Pugh TW, DeFreese DC, et al. Age-specific association of steroid hormone pathway gene polymorphisms with breast cancer risk. *Cancer* 2007;109(10):1940-8.
2. Breast Cancer Association Consortium. Commonly studied single-nucleotide polymorphisms and breast cancer: results from the Breast Cancer Association Consortium. *J Natl Cancer Inst* 2006;98(19):1382-96.
3. Pharoah P. How not to interpret a P value? *J Natl Cancer Inst* 2007;99(4):332-3.
4. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. *Nature* 2007;447(7145):661-78.