General information

- Germline pathogenic variants (PV - including class 4 likely pathogenic and class 5 pathogenic variants) in RAD51D are associated with an increased risk of tubo-ovarian cancer (TOC) and breast cancer (BC)
- The risk varies with extent of cancer-family history
- There is a suggestion that PV in RAD51D are more strongly associated with triple negative (ER, PR and HER2 receptor negative) BC or oestrogen receptor [ER] negative BC. However, this has not been substantiated in all literature.
- The cancer risks are associated with truncating PV in these genes. An association has not been demonstrated for missense variants.

Associated risks

Breast cancer⁷ (risk varies with family history of BC)

- Life time risk: 20% (95% CI 14-28) (female carriers without a significant family history of BC)
- Life time risk: 44% (95% CI 33-55) (two first degree relatives affected with BC)
- Relative risk 1.83 (95% CI 1.24-2.72)

For individual patients we recommend use of tools such as CanRisk* to generate personalised age-specific risks to direct surveillance and risk reducing strategies (see below).

Tubo-ovarian cancer⁷ (risk varies with family history of TOC)

- Life time risk: 13% (95% CI 7-23) (female carriers with no family history)
- Life time risk: 36% (95% CI 23-53) (two first-degree relatives affected with TOC at 50 years)
- Relative risk: 7.6 (95% CI 5.61-10.30)

TOC risk peaks between 50-69 years of age (although age specific results were based on small numbers). Individualised age-specific risk scores can be obtained through tools such as CanRisk*.

Management recommendations

Surveillance⁷

- **Breast:** Should be based on individualised risk assessment using tools such as CanRisk*, and in accordance with NICE guidelines on familial breast cancer (CG164).
  - Moderate risk surveillance (lifetime risk of 17-29%): annual mammograms 40-49 years then NHBSP
  - High risk surveillance (lifetime risk of ≥30% but <40%): annual mammograms 40-59 years then NHBSP
  - Very high risk screening (lifetime risk of ≥40% and 10-year risk of 8% 25-29 yrs, 30-39 years or 12% 40-49 years): refer to VHR breast screening programme

- **Tubo-Ovarian:** Not currently recommended. No evidence-based screening programme. Should be offered only as part of an ethically approved research study.

Risk reducing surgery⁷

- **Breast:** Consider discussion of risk-reducing mastectomy if lifetime risk >30%, in conjunction with an individualised risk assessment* and appropriate counselling.

- **Tubo-Ovarian:** For RAD51D carriers with ≥5% lifetime risk, RRSO should be considered from 50 years. It can be considered in carriers younger than 50 years following individualised risk assessment*, including assessment of menopausal symptoms and shared decision making.

Lifestyle advice

- Provide information about regular self breast examination and ovarian cancer symptom awareness.
- Provide information on the benefits of smoking cessation, minimising alcohol intake and maintaining a healthy weight to lower the chance of getting cancer.
- Contraception: Use of oral contraceptive pill (OCP) is not contraindicated. No specific studies of OCP use in RAD51D carriers have been undertaken. Population studies suggest OCP use may reduce the risk of developing ovarian cancer. There have been conflicting studies on breast cancer risk with OCP but recent studies suggest that OCP use does not significantly increase risk in women at increased familial risk.

Family matters

- Refer to clinical genetics to facilitate genetic testing in at-risk family members.
- Refer to clinical genetics for discussions on reproductive options.

References


*Individualised breast, contralateral breast and ovarian cancer risk estimates which incorporate germline PV carrier status, personal risk factors and where relevant breast cancer chest status, polycystic ovary score and breast density, are available at [https://canrisk.org/](https://canrisk.org/) (Lee et al., 2021)

Patient resources

- breastcancernow.org – Someone like me: [https://breastcancernow.org/information-support/support-you/someone-me-telephone-support](https://breastcancernow.org/information-support/support-you/someone-me-telephone-support)
- Coppafeel [https://coppafeel.org/](https://coppafeel.org/)

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