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Evaluating the oncological safety of hormone replacement therapy in *BRCA* alteration carriers who have undergone a bilateral oophorectomy: a systematic review and meta-analysis

Aoife Nohilly, Matthew Davey, Luis Bouz Mkabaah, Michael Kerin, Aoife Lowery

Discipline of Surgery, Lambe Institute for Translational Research, University of Galway, Galway, Ireland

Background: Patients with BReast CAncer (*BRCA*) gene alterations are recommended to undergo a prophylactic bilateral oophorectomy (PBO). While hormone replacement therapy (HRT) is offered following surgery to alleviate menopause symptoms, it has also been shown to increase breast and endometrial cancer risk.

Methods: A systematic review of prospective studies was performed as per the PRISMA guidelines. Dichotomous variables were analysed the Mantel Haenszel method using RevMan 5.4 software. Subsequent cancer diagnoses (SCDs) were defined as a subsequent breast or endometrial malignancy diagnosed after commencing HRT.

Results: Six studies including 1,841 *BRCA* alteration carriers patients who had undergone a PBO were included. Of these, 45.79% (843/1,841) were prescribed HRT. SCDs were similar irrespective of HRT use [odds ratio (OR): 0.93, 95% confidence interval (95% CI): 0.70–1.23, $P=0.60$, heterogeneity ($I^2=47\%$)]. For patients who had oestrogen only HRT (OHRT), SCDs were also similar (OR: 0.66, 95% CI: 0.41–1.07, $P=0.09$, $I^2=0\%$). For patients who had combined hormone replacement therapy (CHRT), SCDs were also similar (OR: 1.31, 95% CI: 0.81–2.11, $P=0.27$, $I^2=60\%$). Patients in receipt of CHRT had less SCD relative

to those in receipt of CHRT (OR: 0.52, 95% CI: 0.28–0.96, $P=0.04$, $I^2=56\%$).

Conclusions: In *BRCA* alteration carriers who have undergone PBO, HRT prescription did not increase SCD, however, patients who received CHRT had a significant reduction in SCD compared to those with OHRT. Therefore, CHRT provides the safest oncological outcomes in *BRCA* alteration carriers who have undergone PBO.

Keywords: Bilateral oophorectomy; BReast CAncer (*BRCA*); breast cancer; hormone replacement therapy (HRT); oncological safety

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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