

Survival Outcomes With or Without Risk Reducing Mastectomy in *BRCA1* & *BRCA2* Pathogenic Variants Carriers

D Gareth Evans^{2, 3, 5, 7}, Sacha Howell^{1, 2, 3, 6}, Elaine Harkness⁴, Emma Woodward⁵, Fiona Lalloo⁵, Claire Forde⁵, James Harvey^{2, 3}, Lyndsey Highton², Nicola Flaum^{1, 6}, Ashu Gandhi^{1, 2}

1 Division of Cancer Sciences, Faculty of Biology, Medicine & Health, University of Manchester, UK; 2 Manchester University Hospitals, Manchester, UK; 3 Manchester Academic Health Sciences Centre & Manchester Breast Centre, University of Manchester, Manchester, UK; 4 Division of Informatics, Imaging and Data Sciences, The University of Manchester, Manchester, UK; 5 Manchester Centre for Genomic Medicine, Manchester University Hospitals NHS Foundation Trust, Manchester, United Kingdom 6 Christie Hospital NHS Foundation Trust, Manchester, UK; 7 Division of Evolution, Infection and Genomic Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester

ABSTRACT

Purpose Many women carrying pathogenic variants of *BRCA1* and *BRCA2* genes (pv*BRCA1/2*) elect to undergo bilateral risk-reducing mastectomy (BRRM) in the belief that it will improve their overall survival. Whilst many are satisfied with their decision to undergo BRRM a significant minority exhibit regret. We compared long-term oncology outcomes in women with pv*BRCA1/2* choosing BRRM with those choosing a program of imaging surveillance.

Patients & Methods All participants were attendees at a regional family history/genetics service and had undergone genetic testing for pv*BRCA1/2*. Carriers of pv*BRCA1/2* elected either to undergo BRRM or imaging surveillance as directed by UK national guidance. A prospective cohort design examined overall survival, breast cancer specific death and breast cancer incidence between the study groups.

Results A total of 460 women elected to undergo BRRM whilst 745 chose surveillance (mean ages 38.5y & 40.9y respectively; $P=ns$). Follow-up totalled 4652 woman-years. Overall annual incidence rate of breast cancer was 2.4%, falling to 0.15% following BRRM, a 94% reduction compared to surveillance alone (log-rank chi-square=86.1 $P<0.001$). There were 9 prevalent cancers diagnosed at BRRM group (2%). Breast cancer specific deaths were similar in the BRRM and surveillance groups (2 and 4 deaths respectively; $P=ns$; 4634 and 5419 years of woman-follow-up respectively). Proportionately, more women die from ovarian than from breast cancer in both treatment groups.

Conclusion For women electing imaging surveillance over risk reducing surgery our results may offer reassurance that their breast cancer specific and overall survival is unlikely to be compromised. However, breast cancer incidence rates are significantly reduced following BRRM compared to imaging surveillance, which may be important information for women with pv*BRCA1/2* considering BRRM.