Germline BRCA1 and BRCA2 variants in a population-based cohort of ovarian, peritoneal or fallopian tube cancer patients in Malaysia


1 Cancer Research Malaysia, Selangor, Malaysia
2 Genetic Epidemiology Laboratory, Department of Pathology, The University of Melbourne, Australia
3 Victorian Life Sciences Computation Initiative, Melbourne, Australia
4 Department of Computing and Information Systems, The University of Melbourne, Australia
5 Precision Medicine, School of Clinical Sciences at Monash Health, Monash University, Australia
6 Gleneagles Penang, Penang, Malaysia
7 Hospital Ampang, Kuala Lumpur Malaysia
8 Hospital Sultan Ismail, Johor, Malaysia
9 Hospital Kuala Lumpur, Kuala Lumpur, Malaysia
10 Hospital Sultanah Bahiyah, Johor, Malaysia
11 Hospital Tengku Ampuan Afzan, Pahang, Malaysia
12 Institut Kanser Negara, Putrajaya, Malaysia
13 KPJ Johor Specialist Centre, Johor, Malaysia
14 KPJ Sabah Specialist Centre, Sabah, Malaysia
15 Loh Guan Lye Specialist Centre, Penang, Malaysia
16 Hospital Likas, Sabah, Malaysia
17 Pantai Hospital Kuala Lumpur, Kuala Lumpur, Malaysia
18 Subang Jaya Medical Centre, Selangor, Malaysia
19 Sarawak General Hospital, Sarawak, Malaysia
20 University Malaya Medical Centre, Kuala Lumpur, Malaysia

Abstract: Background: Germline BRCA1 or BRCA2 pathogenic variants in ovarian cancer patients may be predictive of sensitivity to platinum derivatives and PARP enzyme inhibitors. Population studies have indicated a >10% prevalence of BRCA1/2 pathogenic variants with wide variance amongst ethnically different populations. We aim to establish the first population-based cohort to assess the prevalence of BRCA1/2 in ovarian cancer patients throughout Malaysia. Methods: From August 2016, women with non-mucinous epithelial ovarian, peritoneal or fallopian tube cancer are continually being recruited to the MaGiC Observational Study. DNA were tested using a Hi-Plex next generation sequencing method and multiplex ligation-dependent probe amplification to detect <10bp alterations and exon deletions/duplications in the BRCA1 and BRCA2 genes. Results: Interim results from 208 patients tested until September 2017 have identified BRCA1 and BRCA2 pathogenic variants in 10.1% (21/208) and 2.9% (6/208) patients, respectively. Variants of uncertain significance were detected in 15.9% (33/208) patients and no pathogenic variants were detected in 71.2% (148/208) patients. Taken together, the prevalence of BRCA1/2 in ovarian cancer patients is...
approximately 13.0% (27/208). **Conclusions:** To our knowledge, this will be the first population-based cohort of Malaysian women with ovarian, fallopian tube or peritoneal carcinoma. Given the clinical significance of *BRCA1/2* pathogenic variants in patient management and cancer risk assessment, the data arising from this study may be beneficial to healthcare professionals in medical practice and genetic service centres in Malaysia. NMRR-16-1322-31114, UMMC 20163-2255 and RSDH 201612.2.

**Keywords:** ovarian cancer; peritoneal cancer; fallopian tube cancer; prevalence


*Correspondence to: Joanna Lim. Cancer Research Malaysia, Selangor, Malaysia; joanna.lim@cancerresearch.my*