Background

PALB2 is considered to be a moderate- to- high-penetrance breast cancer predisposition gene, and recently revised National Comprehensive Cancer Network (NCCN) 1.2016 Guidelines recommend that PALB2 mutation carriers undergo an annual breast MRI and consider surgical prophylaxis. Growing implementation of multigene hereditary breast cancer panels is expected to discover more patients with moderate-to-high penetrance gene findings. Our study describes the clinical presentation of 77 PALB2 mutation carriers and reviews risk-management considerations for the purpose of helping clinicians prepare themselves and their patients to deal with actionable results.

Methods

Seventy-seven (77) sequential patients who had been referred for genetic testing were selected based on the identification of a Pathogenic or Likely Pathogenic (P/LP) variant in PALB2 and on a personal history of cancer. De-identified personal and family histories that had been provided by ordering clinicians were examined.

Results

Clinical characteristics of 77 PALB2-positive patients (% of total)

- Positive Family History (56/77)
- Multiple Primaries (21/77)
- TNBC (9/77)
- < 50 Years at Age of Onset (36/77)
- Positive Family History (56/77)
- Multiple Primaries (21/77)
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Conclusions

- Based on recent revisions to NCCN Guidelines, management of PALB2-positive patients includes breast MRI and consideration of risk-reducing mastectomy.

- This patient series highlights clinical aspects of PALB2-related breast cancer suggestive of a high-penetrance gene, including presentation of early-onset and multiple primary cancers.

- PALB2 is mutated in the germline of roughly 1% of appropriately tested patients. It confers lifetime breast cancer risks from 30% to 60% based on family history (Antoniou, AC, et al. NEJM. 2014; 371(6):497-506), which, at the high end, is comparable to risk from BRCA2.

- More research is needed to understand the relationship between PALB2 and other cancers.

Limitations of study: ascertainment bias, limited information on tumor pathology/hormone receptor status, and an unconfirmed family history.