Patient ID	Variant detail	Age at diagnosis	Tumor IHC	Histopathology	Secondary cancer, age	Family History
1	*MLH1, NM_000249.3, Deletion (Exons 16-19)*	43	ER+/PR+, HER2-	IDC Grade II	Ca Colon	father, ca colon
2	*MSH6, NM_000179.2, c.3261del (p. F1088Sfs*2)* *BRCA1, NM_007294.3, Deletion (Exons 1-2)*	30	Triple Negative Disease	IDC Grade III	-	mother, maternal aunts, grandmother, ca breast and uterine
3	*MLH1*, NM_000249.3, Exon 3, c.306G>T (p. E102D)	39	ER+/PR+, HER2-	IDC Grade II	-	sister, ca breast
4	*MLH1*, NM_000249.3, Intron 16, c.1897-2A>G	60	Triple Negative Disease	IDC (Grade not available)	-	sister, cousins, ca breast
5	*MSH6*, NM_000179.2, Exon 4 c.1222_1226del (p.P408Dfs*8),	30	ER-/PR-, HER2+	DCIS	-	Negative

IHC= Immunohistochemistry, IDC= Invasive Ductal Carcinoma, DCIS= In-situ Ductal Carcinoma, ER= estrogen receptor, PR=progesterone receptor HER2= Human Epidermal Growth Factor Receptor 2

https://doi.org/10.1016/j.gim.2022.01.077

eP040

Breast cancer patients categorized as high-risk of recurrence and/or basal-type molecular subtype by Agendia should universally undergo germline genetic testing

Brenna Bentley[1], Chloe Wernecke[1], Kelly Bontempo[1], Maureen Graham[1], Pat Whitworth[2], Rakesh Patel[1], Peter Beitsch[1]

[1]*Medneon;* [2]*TME*

Introduction: With the rise of somatic testing, more physicians are using panels to understand the genetic profile of breast cancer to help aid in clinical management. Agendia, a molecular diagnostics company focused on breast cancer, has developed two tests to support clinical decisions. MammaPrint analyzes 70 genes associated with breast cancer recurrence and reports whether an individual has a low (1.3%) or high (11.7%) risk for recurrence. BluePrint analyzes 80 genes to identify the breast cancer's molecular subtype: Luminal A (low-risk), Luminal B (high-risk), HER2 (respond well to HER2-targeted therapies), and Basal-Type (aggressive subtype). However, little is known about the relationship between the results of Agendia's tests and the likelihood of identifying an underlying germline variant. We hypothesize that individuals in the High-Risk category on MammaPrint, and individuals with Basal subtype are more likely to have positive germline genetic results indicating the presence of a pathogenic or likely pathogenic variant.
Methods: Patient data was obtained from the Informed Genetics Annotated Patient Registry (iGAP), an IRB-approved multi-centered longitudinal, observational study designed to capture genetic and genomic test results and their utilization and impact on treatment practices and outcomes to help determine the most effective use of testing in real-world patient populations and to support access to advances in precision medicine. Of the 2,439 subjects currently enrolled in the registry, 1,231 have been diagnosed with breast cancer (50.47%). 267 individuals underwent tumor profiling through Agendia's MammaPrint and/or BluePrint as well as germline genetic testing. Descriptive statistics were used to assess and compare data of these populations.
Results: Results indicate that of the 267 individuals who were tested through Agendia's MammaPrint (239) and/or BluePrint (127) panels and underwent germline genetic testing, 135 (56.49%) were classified as High-Risk for recurrence on MammaPrint, and 104 (45.51%) were identified as having a Low-Risk for recurrence. Individuals with a high-risk of recurrence had a 10.04% positive germline variant rate compared to the low-risk group with a 5.44% positive rate. 127 individuals with breast cancer were tested and categorized through Agendia's BluePrint panel. Eight were classified as Basal type, 2 as HER2 type, 58 as Luminal A type, 35 as Luminal B type, and 24 a Luminal type unspecified. Individuals with Luminal A type had the highest positive germline rate of 45.67%, compared to HER2 (1.57%), Basal (6.30%), Luminal B (27.56%), and Luminal unspecified (18.90%).
Conclusion: The iGAP real-world evidence database revealed that individuals categorized as having a high risk of breast cancer recurrence through Agendia's MammaPrint were identified to harbor a pathogenic or likely pathogenic variant 10.04% of the time. An even higher likelihood (45.67%, 27.56%, and 18.90%) was seen in individuals with a Luminal A, Luminal B, and Luminal unspecified molecular subtype, respectively. This data argues that germline genetic testing should be offered to every individual, regardless of age, identified as having a high risk of breast cancer recurrence and/or a Luminal-type molecular subtype on Agendia's tests. Identification of a pathogenic or likely pathogenic variant has clinical management, familial, and potentially reproductive implications.

https://doi.org/10.1016/j.gim.2022.01.078

eP041

How long will they wait? Applying updated NCCN criteria to previously unqualified patients reveals missed opportunities for personalized cancer management

Kelly Bontempo[1], Eric Brown[2], Chloe Wernecke[1], Brenna Bentley[1], Krista Ortega[1], Jessica Kreamer[3], Peter Beitsch[2], Rakesh Patel[2]

[1]*Medneon;* [2]*Targeted Medical Education;* [3]*Northwestern University*

Introduction: Uncovering germline genetic variants responsible for cancer predisposition allows providers to implement personalized medical care for patients. The NCCN Guidelines were designed to help identify individuals who qualify for genetic testing, yet multiple studies have shown that approximately half of patients with pathogenic or likely pathogenic variants are missed using these guidelines. While guidelines have continued to evolve as more robust data have