Findings Beyond BRCA 1/2 Impact Management of Hereditary Breast and Ovarian Cancer Families

Lindsay Kipnis (DFCI) , Jilliane Sotelo (DFCI), Anu Chittenden (DFCI), Jill Stopfer (DFCI) , Katherine Schneider (DFCI), Rosalba Sacca (DFCI), Samantha Culver (DFCI), Diane Koeller (DFCI), Shraddha Gaonkar (DFCI), Erica Vaccari (DFCI), Sarah Cochrane (DFCI), Whitney Espinel* (HCI), Marjan Champine (HCI), Heather Hampel (OSU), Joanne Jeter (OSU), Kevin Sweet (OSU), Robert Pilarski (OSU), Rachel Pearlman (OSU), Kate Shane (OSU), Pamela Brock (OSU), Judith Westman (OSU), Scott T. Michalski (Invitae), Edward D. Esplin (Invitae) *Presenting Author

BACKGROUND

- Clinical utility of germline genetic testing for *BRCA1* and *BRCA2* has long been established. However, management recommendations for pathogenic variants in other genes, typically included in multigene panels, have only recently been included in consensus guidelines.
- Clinician actions implemented for findings in these genes, and patient follow-up, are not yet well studied.
- Results reported from a multi-site study of provider recommendations and clinical actions undertaken in patients with clinical presentations concerning for HBOC and carrying a pathogenic mutation in cancer risk genes other than *BRCA1/2*.

METHODS:

- Retrospective examination of 2,184 patients with a personal history consistent with HBOC.
- Referred to Invitae for hereditary cancer multigene testing from three major academic medical centers.
- Study included de-identified case report forms from 21 clinicians across 3 academic medical centers.
- 104 participants had pathogenic findings in a non-*BRCA1/BRCA2* cancer risk gene & associated survey follow up (figure 1).
- Ordering clinicians completed a short case report form describing the clinical actions taken and patient follow-up up to 36 months post testing.

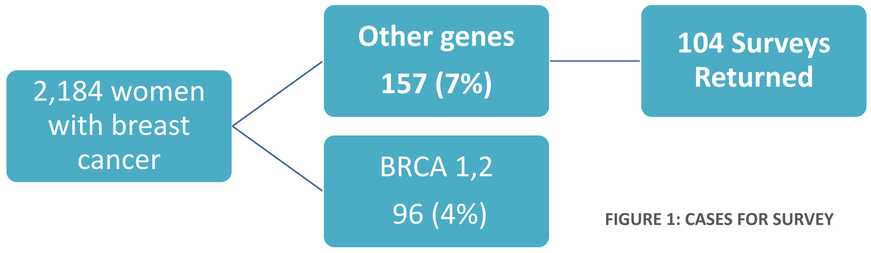


FIGURE 1: CASES FOR SURVEY

RESULTS: VARIANT BASED PROVIDER RECOMMENDATIONS

- Provider made additional result- based clinical recommendations, or altered counseling in 61 probands and for relatives in 66 families.
- This included a total of 72 unique recommendations for probands and 141 recommendations for family members of these individuals (figure 2a and 2b).

FIGURE 2A: PROBAND RECOMMENDATIONS

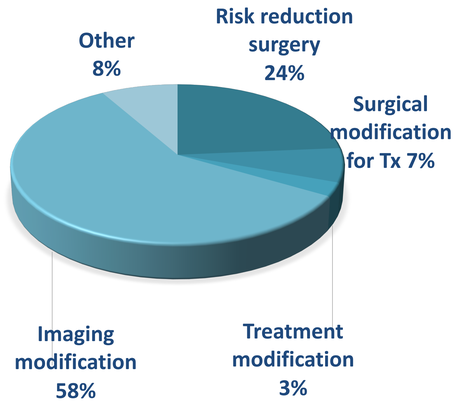
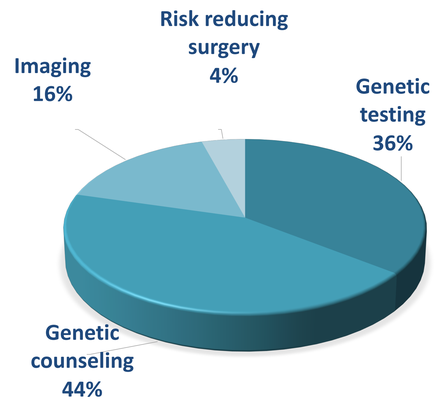


FIGURE 2B: FAMILY RECOMMENDATIONS



RESULTS: A BROAD SPECTRUM OF CLINICAL IMPLICATIONS

- In 28/61 patients with results based recommendations, the variant occurred in a gene associated with moderate cancer risk (figure 3).

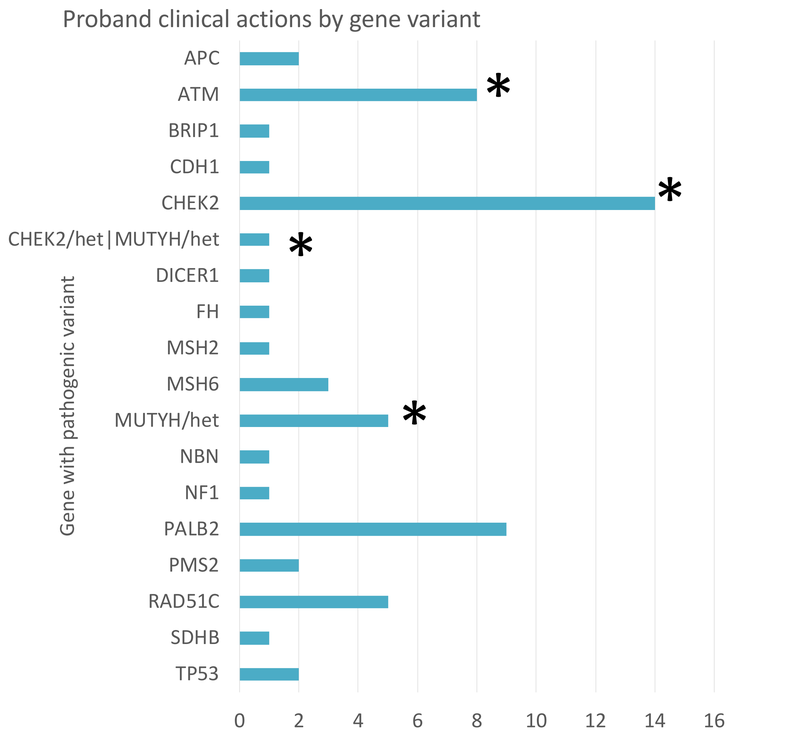


FIGURE 3: VARIANT-BASED CLINICAL RECOMMENDATIONS
* RECOMMENDATION IN MODERATE CANCER RISK GENE

RESULTS: ACTION AFTER PROVIDER RECOMMENDATIONS

- Proband recommendations were carried out in 40/61 individuals. For 14 changes were unknown and 7 reported no changes

52 results-based actions taken by probands included:

- 62% imaging surveillance protocol
- 17% prophylactic surgery
- 10% modification of treatment
- 11% other actions were taken.

44 results based actions for family members included:

- 54% genetic counseling and testing
- 39% imaging surveillance protocol
- 5% surgical prophylaxis
- 2% chemoprevention

RESULTS: POSITIVE RESULTS WITH NO IMPACT ON RECOMMENDATIONS

- In 42 patients, results did not impact recommendations (table 1).
- In two TP53 cases, the provider decided results were likely due to a hematologic process and not germline risk.

Patient had advanced stage cancer	9
Cancer treatment dictated management	5
Result based management guidelines do not exist	5
Patient already managed as high risk	5
Result deemed not related to germline risk	3
Not specified	15

Table 1: Clinician Recommendations NOT impacted by positive results (n= 42 patients)

CONCLUSIONS

- For the majority of patients and family members providers made medical recommendations or counseled differently than they would have if testing would have not been performed.
- Individuals receiving results-based recommendations frequently implemented provider recommendations, indicating results from expanded panel testing are impacting patient care.
- Results emphasize the need for insurers to reimburse clinically impactful testing and the need for medical management guidelines to address a broad spectrum of possible results with implications for different cancer types.