Submitted by:
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Dear NCCN Guidelines Panel:

On behalf of the TME/Breast Care Network, we respectfully request the *Breast Cancer Panel* to review the enclosed data for your consideration in changing genetic testing guidelines for patients with breast cancer.

TME/Breast Care Network: A group of breast cancer specialists including surgeons, radiation and medical oncologists who conduct research via an academic and community-based network.

Specific Change for Consideration: Recommend that *all* patients who are diagnosed with breast cancer be offered the opportunity to have multi-gene panel testing.

Rationale: In support of the proposed change, we submit our recently published research paper that found that the rate of pathogenic variants is essentially equivalent between patients who meet 2017 testing guidelines and patients who do not meet testing guidelines.

Highlights of our findings include:

- 8.65% of patients had a pathogenic/likely pathogenic (P/LP) variant. Of patients who met 2017 NCCN guidelines with test results, 9.39% had a P/LP variant. Of patients who did not meet guidelines, 7.9% had a P/LP variant. The difference in positive results between these groups was not statistically significant ($p = 0.4241$, Fisher exact test).
- 82% of the variants found have either NCCN or other management guidelines associated with them, including clinical trials that the variant makes the patient eligible for
- Universal testing of all breast cancer patients identified more patients harboring actionable
- variants than restricted testing

Potential benefits:

- Simplify testing guidelines for providers
- Reduce the need for "screening" by the current limited genetic counseling resources leaving this valuable resource: the GC's free to counsel patients with variants or other needs
- Identifying variants in breast cancer patients opens the door for cascade testing of family member offering true opportunities for prevention or early intervention
- Provide additional treatment and management options for patients with breast cancer
- Increase access to the underserved
- Current criteria do not adequately account for the full range of clinical presentations described to date in association with hereditary breast and ovarian cancer; carriers of clinically actionable variants in genes other than *BRCA1/2* are likely to fall outside of current

criteria. Studying all patients will help identify the biologic mechanisms of breast cancer and open the door for more research into effective treatment options.

We have attached our article and the electronic link: http://ascopubs.org/doi/10.1200/JCO.18.01631.

In addition, we are including some references to additional articles that support this proposal:

1. Yang S, Axilbund JE, O'Leary E, et al: Underdiagnosis of hereditary breast and ovarian cancer in Medicare patients: genetic testing criteria miss the mark. Ann Surg Oncol 25:2925, 2018.
2. Tung N, Lin N, Kidd J, et al: Frequency of germline mutations in 25 cancer susceptibility genes in a sequential series of patients with breast cancer. J Clin Oncol 34(13):1460–1468, 2016.
3. Kurian AW, Hare EE, Kingham KE, et al: Clinical evaluation of multiple gene sequencing panel for hereditary cancer risk assessment. J Clin Oncol. 32(19):2001-2009, 2014.
4. Levy-Lahad E, Lahad A, King M-C: Precision medicine meets public health: population screening for BRCA1 and BRCA2. J Natl Cancer Inst 107(1):420, 2015.
5. Childers CP, Childers KK, Maggard-Gibbons M, et al: National estimates of genetic testing in women with a history of breast or ovarian cancer. J Clin Oncol 35(34):3800-3806, 2017

We know you have many considerations when you change guidelines, including resources required to execute the change in a way that will benefit patients. We have considered these and believe:

- Breast specialists who see their patients frequently are in a good position to get patients tested and then directed to the proper follow up resources including genetic counselors
- Genetic testing, unlike other universally offered screening tests that are done frequently, is done once in a lifetime and can be valuable over the lifetime of the patient

We are happy to provide additional references and other resources if you would like. Thank you for your consideration and for the important work that you continue to do at the NCCN.

Sincerely,

Dr. Peter Beitsch
Primary Investigator