TITLE: Yield of Multi-Gene Testing in Affected and Unaffected Patients Meeting NCCN *BRCA1/2* Testing Criteria

AUTHORS: Leslie Bucheit, MS, CGC; Kimberly Banks, MS, CGC; Rachel McFarland; Elizabeth Chao, MD, FACMG

PRIMARY CONTACT: Leslie Bucheit, lbucheit@ambrygen.com, Phone 210-441-8973, Fax 949-900-5501

CATEGORY: I – Breast Center Operations, Administration and Programs

SUBCATEGORY: C4 – High Risk Program

OBJECTIVES: NCCN Guidelines provide criteria for single syndrome genetic testing and state "the decision to use multi-gene testing for patient care should be no different than the rationale for testing a single gene." Adoption of panel testing by clinicians is mixed. Use varies from targeting multiple differential cases to use for all patients meeting testing criteria. We sought to determine the yield of panel testing in the commonly-met NCCN *BRCA* testing criteria.

METHODS: Clinical histories of patients who had panel testing at Ambry Genetics were evaluated to identify those meeting NCCN criteria. Analyses were restricted to known *BRCA*-negative cases (n=2320) to identify yield of additional genes. Testing included next generation sequencing and deletion/duplication analyses of 5-28 genes. Clinical history was reported by ordering clinicians. Cases were sorted into affected and unaffected cohorts meeting NCCN criteria; family history analyses included first and/or second degree relatives only. Yield of additional genes was compared to *BRCA1/2* yield for each cohort using the Myriad Mutation Prevalence Tables. Statistical analyses were not performed; sample sizes for *BRCA* mutation yields are not published.

RESULTS: Yield by criteria are below ("category: panel yield; *BRCA1/2* yield" where BR=breast cancer; OV=ovarian cancer; UA=unaffected; dx=diagnosed; w/=with).

- BC dx ≤45: 7.0%; 4.7%
- UA w/ 1 relative w/ BC ≤45: 3.3%; 2.6%
- OC any age: 8.3%; 7.7%
- UA w/ 1 relative w/ OC: 5.5%; 3.0%
- BC ≤45 & 1 relative w/ BC ≤45: 9.5%; 10.4%
- UA w/ ≥2 relatives w/ BC ≤45: 3.4%; 5.6%
- OC & 1 relative w/ OC: 10%; 14.7%
- UA w/ ≥2 relatives w/ OC: 4.5%; 5.3%

CONCLUSIONS: Results indicate yield of non-*BRCA* genes is similar to yield of *BRCA1/2* testing and may be higher than *BRCA* among low level of suspicion, single case indications for the NCCN criteria evaluated. Clinicians in High Risk Programs choosing to order panel tests should thus not limit panel testing to high suspicion cases. Results also suggest that NCCN *BRCA* testing criteria could be used as criteria for panel testing.