Background: Multiplex gene sequencing panels (MGP) are increasingly used for assessment of hereditary breast cancer risk. Compared to testing for BRCA1 and BRCA2 (BRCA1/2), only, testing more genes increases the likelihood of identifying a deleterious mutation (DM) and a variant of uncertain significance (VUS), which might cause distress, uncertainty or regret about testing. Little is known about the patient experience of MGP testing.

Methods: We conducted a prospective study of MGP testing, using a panel of 25 genes: APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDO1, CDKN2A, CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTHY, NBN, PALB2, PMS2, PTEN, RAD51C, RAD51D, SMAD4, STK11, and TP53. Participants were enrolled at three medical centers and were eligible if they met standard genetic testing guidelines or if they had a ≥2.5% probability of a DM in any gene on the panel, as calculated by predictive models (e.g. IBS, Penn 1, MYMMP). Participants were surveyed about their experiences with MGP testing including distress and uncertainty at baseline (before test results disclosure) and three months later. The 25-item Multidimensional Impact of Cancer Risk Assessment (MICRA) scale measured distress, uncertainty and positive experiences at three months after testing. We present a planned interim analysis after enrolling 300 of 2000 total participants.

Results: Of 950 participants, 332 (36%) were referred for suspicion of hereditary breast/ovarian cancer syndrome. Overall, 73% were female, 43% were Hispanic and 33% were Spanish-speaking only, for 25%, high school was their highest level of education. A total of 36% had breast cancer, 36% had ovarian cancer, and 7% had another cancer: 11% had a DM and 35% had VUS in one or more genes. At study entry, most participants thought about cancer rarely or not at all (69%, 95% confidence interval (CI) 58%-77%), and few (7%, CI 3%-14%) had thoughts of cancer that affected their daily lives; results were unchanged three months later, after genetic results disclosure. The 25-item Multidimensional Impact of Cancer Risk Assessment (MICRA) scale measured distress, uncertainty and positive experiences at three months after testing. We present a planned interim analysis after enrolling 300 of 2000 total participants.

Conclusions: Among diverse participants of a prospective, multi-center, MGP testing trial, increases detection of mutations by 5%-15%.

Results are complex: more genes = more variants of uncertain significance (VUS)

1. Incomplete st udy sample (goal: N=2000)
2. Limited follow-up time (goal:12 months)

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**Eligibility criteria:**
1. No prior genetic testing
2. Age ≥18
3. ≥2.5% mutation probability by risk models

**Recruited:** 2014-2015 at 3 centers (LA County, USC, Stanford);

**interim analysis n=500, 332 breast cancer history**

**Complete study accrual and follow-up**

**Incomplete st udy sample (goal: N=2000)**

**Limited follow-up time (goal:12 months)**

**Next Steps**

Complete study accrual and follow-up

Track clinical outcomes (changes in care):

Screening interventions

Preventive interventions

Assess correlation with genetic test results

Multivariable analysis of survey results

**Test results:** 93% negative, 36% VUS, 11% positive

Survey completion to date: Baseline 86%; 3-month 27%

**Early results not suggestive of distress:**

87% never regretted learning about results

81% wanted all their genetic test results

No increase in intrusive thoughts (p>0.5)

MCIRA results low for distress, uncertainty

The Patient Experience in a Prospective Trial of Multiplex Gene Panel Testing for Cancer Risk

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**Background**

Multiplex gene panel (MGP) use is increasing

15-40 genes instead of only 2 (BRCA1/2)

Increases detection of mutations by 5%-15%

Results are complex: more genes = more variants of uncertain significance (VUS)

**Does MGP testing cause patients distress?**

Conclusions:

Among diverse participants of a prospective, multi-center MGP testing trial, cancer- and genetic-testing-related distress was low at entry and remained low three months later. These results provide no evidence for an increase in distress or uncertainty after MGP. Longer-term follow-up in a larger cohort is underway.

**Diverse (43% Hispanic, 33% high school)**

**Early results not suggestive of distress:**

87% never regretted learning about results

81% wanted all their genetic test results

No increase in intrusive thoughts (p>0.5)

**MCIRA results low for distress, uncertainty**

**Next Steps**

Complete study accrual and follow-up

Track clinical outcomes (changes in care):

Screening interventions

Preventive interventions

Assess correlation with genetic test results

Multivariable analysis of survey results

**I regret learning about my genetic test results**

74

Three months, %

19

Occasionally

4

Frequently

3

Not at all or Rarely

3

A Lot

**Multidimensional Impact of Cancer Risk Assessment (MICRA)**

I regret learning about my genetic test results

Three months, %

87% never regretted learning about results

81% wanted all their genetic test results

No increase in intrusive thoughts (p>0.5)

MCIRA results low for distress, uncertainty

**Results**

Percentages and proportions are rounded to nearest integer.