# CLINICAL PRESENTATIONS OF MMR MUTATION POSITIVE PATIENTS WITH NO PERSONAL OR FAMILY HISTORY OF COLON OR ENDOMETRIAL CANCER

Praveen Kaushik, Brent Evans, Kelsey Moyes, Michelle Landon, Jennifer Saam, Richard Wenstrup

Myriad Genetic Laboratories, Inc., Salt Lake City, UT

## BACKGROUND

- Lynch syndrome is caused by mutations in the MMR genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM*) and is associated with several different cancers, including: colon, endometrial, gastric, ovarian, pancreatic, small bowel, brain, ureter/renal pelvis, hepatobiliary tract, sebaceous adenoma/carcinoma.
- Patients with this syndrome are at the highest risk for colon and endometrial cancer, and therefore the testing criteria for this condition are designed with this in mind.
- The testing criteria for all the MMR genes are the same, despite variations in the penetrance of different genes. For example, the cancer risks associated with a *PMS2* or *MSH6* mutation are lower than cancer risks associated with mutations in *MLH1* or *MSH2*.
- With multi-gene panel testing becoming more common, patients with an atypical clinical presentation may be identified to carry a mutation in the MMR genes.
- This analysis presents the clinical characteristics of Lynch positive patients identified with panel testing with no personal or family history of colon or endometrial cancer, who otherwise may not have undergone testing previously for Lynch syndrome alone.

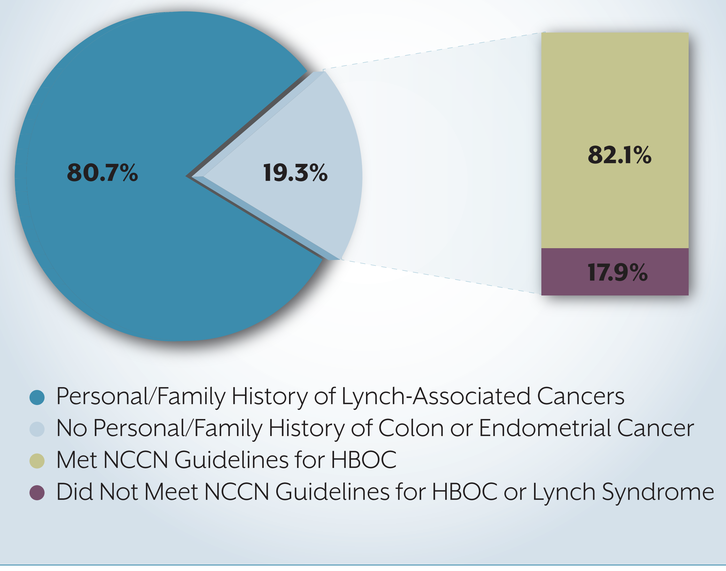
## METHODS

- A retrospective analysis was performed on consecutive patients who tested positive for a deleterious or suspected deleterious mutation in *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM* using the Myriad myRisk™ Hereditary Cancer panel between September 4, 2013 and June 12, 2014.
- Clinical characteristics were reviewed based on data reported on test request forms submitted to a commercial testing laboratory.
- Patients were separated into those who have a personal or family history of colon or endometrial cancer, and those who don't have a personal or family history of colon or endometrial cancer.

## RESULTS

- In this period, 145 patients were identified to carry a mutation in at least one of the MMR genes.
- Thirteen patients (9.0%) did not report a personal or family history of any Lynch-associated cancers but did report a history of other cancers, most notably breast cancer.
- Twenty-eight patients (19.3%) did not report a personal or family history of colon or endometrial cancer. Of these patients:
  - Twenty-three patients (82.1%) met NCCN guidelines for HBOC testing but did not meet the NCCN guidelines for Lynch syndrome testing.
  - Five patients (17.9%) did not meet NCCN guidelines for HBOC or Lynch syndrome.

**Figure 1**
Personal or Family History in Patients with at Least One MMR Gene Mutation




- The 28 patients with no personal or family history of colon or endometrial cancer were found to carry mutations in *MLH1* (n = 3), *MSH2* (n = 5), *MSH6* (n = 10), and *PMS2* (n = 10) (Figure 2).
- Four patients were also found to carry a mutation in two different genes.
  - *ATM* and *MSH2* (n = 1)
  - *MSH6* and *BRCA1* (n = 1)
  - *PMS2* and *BRCA1/BRCA2* (n = 2)

**Figure 2**
MMR Mutations in Patients with No Personal/Family History of Colon or Endometrial Cancer (n=28)

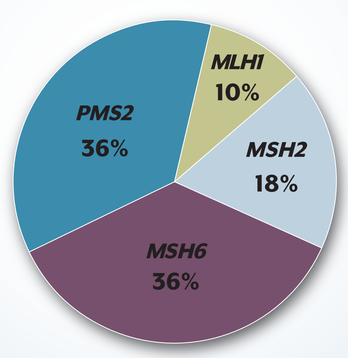
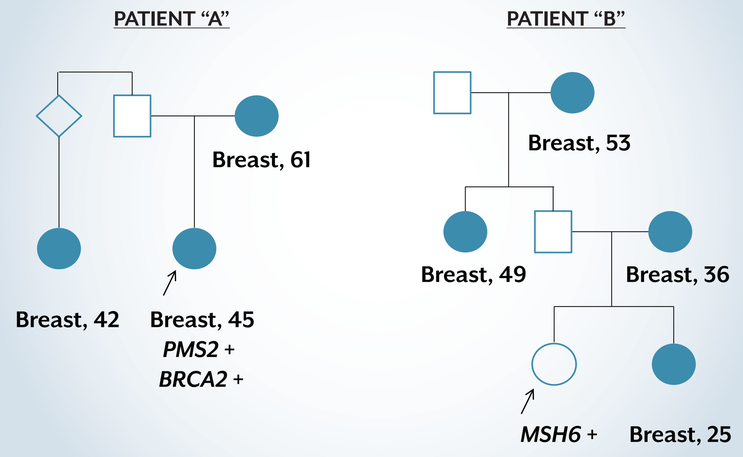



**Figure 3**
Examples of LS Mutation Positive Patients that Didn't Meet NCCN LS Guidelines




## CONCLUSIONS

- This data suggests that a portion of patients with Lynch syndrome may be missed with single syndrome testing practice, specifically patients with mutations in the lower penetrant MMR genes such as *MSH6* and *PMS2*.

Presented at CGA - September 15, 2014