Impact of Multigene Panel Testing on Medical Management: Preliminary results of a pre- and post-genetic testing clinician survey

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Background: Management guidelines have been developed for numerous high and moderate risk colorectal cancer (CRC) predisposition genes. However, limited data currently exist regarding implementation of guidelines based on multigene panel testing (MGPT) results. Here we present data from a survey designed to assess the effect MGPT has on clinical decision making.

Methods: In this web-based study, pre-test surveys were emailed to clinicians upon submission of each MGPT order and post-test surveys were emailed upon results receipt. We then examined cases in which at least one CRC susceptibility gene was tested. Positive results were grouped as high risk (abbreviated HR: *APC, BMPR1A, MLH1, MSH2, MSH6, PMS2*) or moderate risk (MR: *MUTYH* heterozygotes, *APC* I1307K, *CHEK2*), based on the aggressiveness of recommendations in the National Comprehensive Cancer Network v1.2018 Colorectal Genetic/Familial High-Risk Assessment guidelines.

Results: Pre- and post-test surveys were completed by 165 unique providers for 599 cases. Cases with positive or inconclusive findings in genes outside of the HR or MR groups (n=35) were excluded. Of the 564 remaining cases, 45 patients had positive result in the HR or MR groups (8.0%), 106 had inconclusive (8.4%), and 469 had negative results (83.2%). An increase in at least one management option was recommended in most individuals with positive results in HR and MR genes (71.1%), in contrast to those with inconclusive (6.3%) or negative results (8.1%). Amongst 35 MR positives, 65.7% (n=23) had a change in management in any cancer, 10 (28.6%) of which were specific to CRC. Amongst 10 HR positives, 9 had management change specific to CRC and 7 had a change in management for other cancer risks as well.

Conclusions: Preliminary data from this ongoing study demonstrate that positive genetic test results frequently lead to changes in medical management. While MR positive results do not result in changes to CRC management as often as in HR positives, the addition of recommendations for other cancer types supports the clinical utility of pan-cancer MGPT. Encouragingly, increases in management based on negative and inconclusive results are uncommon. Further study is needed to guide clinicians and payers on the impact MGPT has on management and health outcomes of high-risk individuals.