

## Mainstreaming germline genetic testing for men with advanced prostate cancer

**Maria I. Carlo**, Jada Hamilton, Kelsey Breen, Wassim Abida, Karen Autio, Yu Chen, Daniel Danila, Lewis Kampel, Jason Koutcher, Michael Morris, Dana Rathkopf, Susan Slovin, Howard Scher, Mark Robson

Memorial Sloan Kettering Cancer Center

**Background:** About 12% of men with advanced prostate cancer harbor a germline DNA damage response (DDR) gene mutation. Compelling clinical evidence suggests certain DDR mutations may serve as predictive biomarkers for platinum-based therapies or PARP-inhibitors. The National Comprehensive Cancer Network (NCCN) guidelines have added men with biopsy or radiologically proven metastatic prostate cancer as candidates for referral for BRCA1/2 germline testing. Given the large population of patients at risk, and the need to receive timely results for therapy selection, novel methods of delivering clinical genetics testing and results are needed.

**Methods:** We are conducting a prospective, single-arm study to examine an alternative, expedited clinical genetics care delivery model. The aims of this study are to assess whether this approach is safe and acceptable to patients with prostate cancer, and to assess the clinical utility of broad germline testing in this population. During routine medical visits, the patients' oncologists offer genetic testing after standardized pre-test education, which includes a written brochure and video specific for prostate cancer. Genetic testing is performed the same day using a clinically approved and validated multigene panel assay that includes the following: *BRCA1*, *BRCA2*, *CHEK2*, *HOXB13*, *PALB2*, *RAD51D*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM*, *TP53* and *ATM*. Within 2 weeks of consent, patients are asked to complete an email questionnaire. Genetic counselors contact the patient over the telephone for an initial personal and family history assessment, and then again to disclose the results of genetic testing and perform post-test counseling. Patients then complete two additional email questionnaires 1 week and 2 months after receiving results. Optional in-person counseling for patients and their families is also offered to all patients. We define clinical utility if one of three scenarios are met: actual treatment change that would not have occurred without treatment results, future therapy implications, or immediate genetic counseling implications. We assess psychological and behavioral outcomes by patients' self-report in the email questionnaires. The questionnaires assess several constructs including ambiguity aversion, emotional distress, genetics and cancer knowledge, satisfaction with genetic testing.

**Results:** 126 patients have consented to germline testing during routine medical oncology visits. Of these, 109 have already received results. 15 (14%) patients tested positive for a pathogenic or likely pathogenic (P/LP) mutation, and 12 (11%) for a variant of uncertain significance (VUS). P/LP mutations were *BRCA1* (n=3) *BRCA2* (n=5), *CHEK2*, *HOXB13*, *ATM*, and *TP53*. To date, 45 (36%) of patients have completed all questionnaires. Further analysis of clinical characteristics of patients is ongoing and updated results will be presented at the conference.

**Conclusions:** Mainstreaming germline genetic testing to receive timely results appears feasible, with preliminary results showing a significant portion of men harbor germline mutations. Further analysis will indicate whether patients find this approach acceptable.

**Conflict of Interest:** Maria I. Carlo served an advisory role for Pfizer.

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