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threatening. Because clinicians lack tools to make precise predictions of a patient's prognosis, it is often difficult to estimate from which treatment, if any, a man will benefit.

Now a team of Memorial Sloan Kettering researchers — led by <u>Kenneth Offit</u>, Chief of the Clinical Genetics Service; Peter T. Scardino, Chair of the Department of Surgery; <u>Howard Scher</u>, Chief of Genitourinary Oncology; and genetics fellow <u>David Gallagher</u> — reports that the disease often takes an aggressive course in patients who have inherited mutations in the genes *BRCA1* or *BRCA2*.

For two decades, the investigators collected anonymous DNA samples and clinical data from close to 900 prostate cancer patients of Ashkenazi Jewish ancestry, "a substantial resource that now allows us to explore the heritable components of the disease," Dr. Offit explained.

The researchers showed that patients who carry *BRCA* mutations have an increased risk of dying from prostate cancer or having their disease recur after treatment. "Strikingly, we also found that tumors were of more advanced grade in *BRCA2* mutation carriers," Dr. Offit said. "These men are genetically susceptible to a form of prostate cancer that is particularly aggressive."

He and his colleagues are hopeful that the patient group will benefit from a new class of drugs called PARP inhibitors, which are being developed for treatment of *BRCA*-related breast and <u>ovarian cancer</u>. They estimate that such therapy, if proven successful, could be used in treating about 2,800 men with prostate cancer and *BRCA* mutations in the United States yearly.

"However, these patients account for less than 2 percent of all men who suffer from this disease," Dr. Offit noted. He and his colleagues are now exploring whether a type of DNA sequence variation called a single nucleotide polymorphism, many of which are much more common than BRCA mutations, also could help clinicians in determining the prognosis for prostate cancer patients.

The findings were published in the April 1 issue of Clinical Cancer Research. [PubMed Abstract]

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