Hormone Therapy Can Wait in PSA-Only Relapse

By Charlie Schmidt

Men who had prostate cancer can be in for a shock if their prostate-specific antigen (PSA) levels start rising. Only prostate cells release PSA—and in large amounts by those that are cancerous.

When PSA levels rise sharply without other evidence of cancer, it suggests hidden metastatic cells somewhere in the body, beyond sight of modern technologies. Up to 60,000 men face this biochemical relapse every year in the United States—most within 10 years of primary treatment—yet no clinical guidelines exist for how to handle it. One standard approach is to give androgen-deprivation therapy (ADT), which denies prostate cancer cells the testosterone they need to grow. However, ADT has challenging sexual and metabolic side effects. So depending on a patient’s age, anxiety, or other health problems, a doctor might also delay ADT until cancer becomes more evident.

When to start ADT after biochemical recurrence is controversial, and many experts view the decision as a therapeutic dilemma. But mounting evidence suggests that waiting causes no harm. A study presented at the June 2014 annual meeting of the American Society of Clinical Oncology reveals no difference in overall survival between men who delayed ADT after relapse and those who started ADT immediately. According to Xabier Garcia-Albeniz, Ph.D., a research associate at the Harvard School of Public Health in Boston and the study’s lead author, many doctors feel comfortable deferring ADT on the basis of their own clinical experience.

“They see patients doing well without therapy,” he said. “Now these data support their observations.”

“The results show that the timing of ADT doesn’t matter. As long as patients aren’t symptomatic, it’s reasonable to hold off on ADT for as long as possible and spare patients the effects of treatment.”

The levels that define biochemical relapse vary depending on whether patients were treated with radical prostatectomy—which should eliminate PSA from the body—or radiation, which can leave functional prostate tissue intact. According to the American Urological Association, PSA levels of 0.2–0.4 ng/mL in blood predict treatment failure after radical prostatectomy, whereas expert radiology guidelines define biochemical relapse as a level of 2 ng/mL or more over the lowest level identified after radiation treatment.

No Difference in Overall Survival

This observational study investigated 2,022 men tracked by a national cancer registry at the University of California, San Francisco. Some started on ADT within 3 months of relapse, whereas others waited at least 2 years, or until cancer symptoms appeared. Garcia-Albeniz reported that 87.2% of the patients who delayed ADT after relapse were still alive 5 years later, compared with 85.1% of those who waited. Moreover, survival rates stayed similar even among a smaller patient group tracked for nearly 10 years.

All the men were treated initially for nodenegative cancers, which are less aggressive than cancers spreading beyond the prostate.
Identifying Cancer Mutations as Therapeutic Targets

By Anna Azvolinsky

Cancer therapies are increasingly targeting specific molecular pathways and mutations. Molecular testing to identify a mutation expressed in a tumor is becoming common both in clinical research and to gauge whether a patient is eligible for a Food and Drug Administration–approved therapy.

These molecular testing efforts have focused on well-defined pathways that drive tumor growth, such as the phosphatidylinositol 3-kinase (PI3K) and the human epidermal growth factor receptor 2 pathways. And yet researchers are just beginning to understand the genes and pathways important for progression of various tumor types.

Although a diagnostic screening test for a single molecular alteration is increasingly becoming common clinical practice, cancer researchers strive to go beyond this method to provide a wider picture of a tumor’s molecular landscape.

Importance of Single-Patient Studies

Although treatment with targeted therapies often works well initially, many patients develop resistance after chronic exposure to an agent that inhibits a cancer pathway.

“It is fairly well established that there are two major resistance mechanisms: acquired and adaptive resistance,” said Pau Castel, graduate student in the laboratory of José Baselga, M.D., Ph.D., medical oncologist and physician in chief at the Memorial Sloan–Kettering Cancer Center in New York. “[Patients treated with targeted agents who initially respond] tend to acquire adaptive resistance. Tumors are made up of a spectrum of clones and under targeted therapeutic pressure, one...