The Need for Organ Site Specific Cancer Research

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Due to the amount of money available from the DOD, should it support "good basic cancer research" or prioritized prostate cancer specific needs? How would such prostate specific needs be prioritized?

Background

The adult human body is made up of more than seven trillion cells living in harmony in a societal organization, individual responsibilities balanced by societal obligations. Cancer is caused by a series of genetic changes, and those changes result in a very important, deadly biological fact. In normal cells, the rate of production balances the number of cells that die every day. In cancer, the molecular changes lead to the production rate exceeding the loss rate. The cancer continues to grow.

Prostate Cancer

In a well-balanced environment in the prostate, none of the cells are over growing. They are collaborating. When cancer occurs and cancer cells leave the prostate and go to the bone, in those sites it does nothing societally positive. It takes the nutrients, grows and gives nothing back to the host.

Rationale for Organ Site Specific Cancer Research

While cancers within specific organ sites can share a subset of similar malignant changes, there are also unique organ site specific changes not shared with other organ site cancers, which drive their lethality These organ site specific changes are often the best targets for therapies to selectively kill the specific cancer cells without killing the patient.

Due to unique genetic changes, prostate cancer cells acquire the ability for androgen to drive the continuous lethal growth of prostate cancer, which is the basis for androgen ablation therapy. Prostate cancer expresses a series of organ site-specific markers.

.V Prostate Cancer Specific Biomarkers

We oftentimes use PSA as a prognosticator, which is different than a detector. A prognosticator addresses the question of what do I do now that I have been diagnosed with a disease? One of the very interesting things that we don't think a lot about is using PSA as a surrogate marker or intermediate end point.

Prostate cancer biomarkers can be measured in different biological specimens—blood, urine and tissue. There is also a possibility of using biomarkers in functional imaging, which is very important.

Prostate Specific Antigen

PSA was documented to be elevated in the serum in patients with prostate cancer in 1980, and in 1984 the FDA approved serum PSA as a marker for monitoring prostate cancer progression. Ten years later, the FDA approved serum PSA for screening for initial detection of prostate cancer. Currently, 20 million serum PSA tests are done per year in North American plus 20 million outside of North America.

Whole Blood "Liquid Biopsy" for Detection of Circulating Prostate Cancer Cells

More recently, in 2008, the FDA approved the quantitation of the number of circulating tumor cells in the blood to monitor prostate cancer progression using epithelial cells, but not prostate cancer specific markers. This assay can be made prostate cancer specific using prostate cancer specific markers like PSA, PSMA, or unique DNA-based markers.

Effective Therapies

Two distinct phases are required to develop effective therapies for prostate cancer—drug discovery followed by drug development. The drug discovery process, target identification, in vitro testing, animal testing and drug selection, may take as little as two years if everything goes perfectly, but on average it usually takes about five years. You then have a lead candidate as a potential drug, and you go into the process of drug development. The drug development process, which includes drug selection, preclinical toxicity studies, phase I safety studies, phase II efficacy studies, phase III studies and FDA review, takes about 15 years to get a drug to approval. If you add up the cost, it costs roughly $300 million for the drug development process, but if you include the cost of drugs that don't make it through the process, the cost gets up into billions of dollars.

One of the problems with the current drug development process is the blind survival response criteria in phase III clinical trials, which doesn't take into account the under appreciated partial response. The baby is thrown out with the bath water. An urgent need is some type of functional imaging to allow clinicians to assess individual metastatic sites in individual patients. That is a need that is not going to be met by industry.