Clinical Cancer Advances 2006: Major Research Advances in Cancer Treatment, Prevention, and Screening

2006 marked a year of some of the most exciting advances in cancer therapeutics. Never before were so many targeted therapies shown to improve disease-free survival for a wide variety of cancers. The US Food and Drug Administration (FDA) approved several new medical therapies. Many new agents are in clinical trials, and bench research is thriving.

To commemorate the year, ASCO leaders and investigators released the 2006 annual report "Clinical Cancer Advances 2006: Major Research Advances in Cancer Treatment, Prevention, and Screening" last December. The full report can be accessed online at www.asco.org.¹

Uncertain Funding Dampens Enthusiasm About Advances in Cancer Research

The report highlights numerous research advances, but it is cautionary: the authors question whether bench research and clinical trials will continue to accelerate if funding from the National Institutes of Health does not increase annually with inflation. The NIH has experienced a 13% loss in purchasing power since 2003, and the president has proposed slight decreases in funding for fiscal year 2008.

Authors of the report consisted of 20 oncologists, two of whom served as executive editors. They are Robert Ozols, MD, PhD, chair of ASCO's Cancer Communications Committee and Senior Vice President for Medical Science at Fox Chase Cancer Center (Philadelphia, Pennsylvania); and Roy S. Herbst, MD, PhD, Immediate Past Chair of ASCO's Cancer Communication Committee and Chief of the Section of Thoracic Medical Oncology at The University of Texas M.D. Anderson Cancer Center (Houston, Texas).

The report highlights progress made in blood and lymphatic cancers, breast cancers, CNS tumors, gastrointestinal cancers, genitourinary cancers, gynecologic cancers, head and neck cancer, lung cancer, pediatric cancers, and skin cancer between November 2005 and October 2006.

Prevention

The report draws attention to approval of the first cervical cancer vaccine, Gardasil (Merck & Co Inc, Whitehouse Station, New Jersey), which demonstrates 100% effectiveness against human papilloma virus (HPV) 16 and 18. These strains account for approximately 70% of cervical cancers. Many media outlets have listed the cervical cancer vaccine as one of the top-10 health stories of 2006, and 2007 will be a year marked by ramped-up efforts to vaccinate girls and women between the ages of 11 and 26 years, especially preteens who have not become sexually active. The vaccine is

not effective in combating pre-existing infection, but investigators say that it is still worthwhile for women who have become sexually active. It has not been tested in boys, but studies are underway. So far, studies have shown that the vaccine is effective for 3 to 5 years. Its durability and the need for booster shots are being examined.

Kidney Cancer

Another success story concerns treatments for advanced kidney cancer, which are the first new treatments developed in more than 20 years. According to Gabriel N. Hortobagyi, MD, ASCO President and Chair of Breast Medical Oncology at The University of Texas M.D. Anderson Cancer Center, "clinicians need to realize that we no longer should tell patients that there is nothing we can do because there are two new targeted therapies out there."

Clinical trials demonstrated that the addition of the angiogenesis inhibitor sunitinib to interferon boosted progression-free survival and response rates. The investigational drug temsiroleimus also improved survival for people with advanced, high-risk kidney cancer. The report underscores the need for oncologists and primary care physicians to abandon the notion that nothing can be done in the setting of advanced kidney cancer. These drugs are now being offered as part of the standard of care for these patients, while they continue to be studied in the adjuvant setting.

Breast Cancer

The future for treating women who have trastuzumab-resistant breast cancer looks brighter. Results from an international phase III clinical trial of oral lapatinib plus capecitabine among women with treatment-refractory locally advanced or metastatic breast cancer after a course of trastuzumab showed marked extensions in progression-free survival. Median progression-free survival doubled from 17.9 weeks taking capecitabine monotherapy versus 36.9 weeks in the combination treatment arm. The FDA is reviewing an application for approval for use of lapatinib for women who did not respond to trastuzumab and other previous therapies. This will give women with treatment refractory human epidermal growth factor receptor 2 (HER-2) positive breast cancer a new treatment option. Dr Hortobagyi urged oncologists to follow these studies because of their potential to change the standard of care.

Head and Neck Cancer

Like kidney cancer, head and neck cancer has been characterized by a lack of effective treatment options. Until

2006, there was a 45-year hiatus in treatments for head and neck cancer.

Results from a multinational study revealed that patients treated with the combination of cetuximab and radiation therapy lived for an average of 49 months, compared with 29.3 months among patients treated with standard radiation therapy alone. In 2006, the FDA approved cetuximab as a first-line therapy with radiation therapy for patients with head and neck cancer that are not suitable candidates for surgery. Cetuximab is also approved for patients who are no longer responsive to chemotherapy.

Lung Cancer

Discovery of the new genetic test to predict lung cancer prognosis, called the “lung metagene model,” was a milestone in 2006. The test is able to stratify patients with stage 1A cancer who would be most likely to benefit from chemotherapy after surgery. Although the accuracy of the test is approximately 72% to 79%, it was more accurate than clinical characteristics, such as tumor size alone. Further study will determine whether the test should alter the standard of care.

Hematologic Cancers

The outcome for patients with cancers of the blood and lymphatic system that are resistant to imatinib is improving with the FDA approval of dasatinib for chronic myelogenous leukemia in June 2006.

Similarly, the outlook for patients with advanced follicular lymphoma is improving. A phase III trial revealed that two years of maintenance therapy with the monoclonal antibody rituximab after chemotherapy slowed disease progression and improved disease-free survival. Fifty-six percent of patients showed no evidence of disease at a follow-up of four years with maintenance rituximab, compared with 33% of patients who underwent chemotherapy alone. Survival data also showed an added benefit. At four years, 88% of the patients on rituximab were still alive after four years, compared with 72% of the observation group.

Even though skeptics have questioned the high cost of some of these targeted therapies, the report said that breakthroughs in science are permitting stratification of patients so that the drugs are not overused.

A case in point reveals how research into HER-2 has shown that only women who are HER-2 positive stand to benefit from Herceptin. Since approximately 20% to 25% of women are HER-2 positive, the standard of care is to limit Herceptin to this group. The report underscored how the ability to stratify and treat patients based on their unique personalized characteristics (eg, pharmacogenomic and proteomic profile) is an area that is no longer on the horizon.

In forecasting where cancer research is headed, Dr Hortobagyi adds a note of caution. “These advances did not happen by accident,” he said. “These are the results of 30 years of work by investigators, and by a major investment this country has made in cancer research.” ASCO leadership is pressing for a floor of at least a 5% increase for further research, not including additional funds to translate research findings from the bench to the bedside.

Issues Affecting Research

Biospecimens

Obtaining and storing biospecimens is seriously hindering research, noted Dr Hortobagyi. At issue is the absence of standardized procedures for collecting, storing, and accessing biospecimens on a national level. The National Cancer Institute’s effort to establish and maintain biorepositories is a crucial first step, but implementation will require funding and more specific guidance. To expedite research, the ASCO report presses for establishing a nationally-available database linking all biorepositories. Like the National Human Genome Project, the proposed database would facilitate sharing information and expertise across institutions.

Tissue Ownership and Intellectual Property

Debate over tissue ownership and intellectual property rights has also limited biospecimen access. ASCO leadership recommends the development of a collaborative effort, bringing together all the stakeholders (investigators, cancer institutions, government, industry, and patient groups). The major objective of such a collaboration would be to sort out ways to share data, while assuring appropriate protection for intellectual property.

Patient Privacy

Privacy laws, notably the Health Insurance Portability and Accountability Act (HIPAA) have made the conduct of research significantly more complex. Authors of the report say that they support the overall principles of HIPAA, but are concerned about the effect of variations in implementation and interpretation.

Securing authorization (in addition to consent) from each patient to use the information for research is a new requirement mandated by HIPAA. According to Dr Hortobagyi, the impact of HIPAA on advancing clinical research should be analyzed.

Indeed, the report calls attention to an Institute of Medicine (IOM) report that flagged many key problems, and ASCO recommends that IOM conduct additional review. Among the IOM panel’s concerns were how HIPAA has ratcheted up the costs of research, made the research endeavor far more time-consuming, and enhanced fears of liability. These issues have resulted in some institutions withdrawing from research

efforts and in marked reduction in patient participation in cancer registries.

The infrastructure for funding clinical research is critical to continued research progress. Maintaining that infrastructure requires funding that keeps pace with inflation, according to ASCO Executive Vice President and CEO Allen S. Lichter, MD.

Until 2003, funding through the National Institutes of Health rose steadily, but it has not increased since then. If

you look squarely at the impact of this plateau, said Dr Lichter, “what you see are stalled programs, bottlenecks in translating discoveries to the clinic, less innovation, fewer clinical trials, stopping trials without completing them, and seeing more young brilliant researchers leaving the field.”

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Reference

1. Clinical Cancer Advances 2006. Available at: http://www.plwc.org/PLWC/ASCO%20Resources/Research%20and%20Meetings/CCA_2006.pdf

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