**Yale Cancer Center Carves New Path in Immunotherapy**


Cancer immunotherapy is showing promise in treating patients with a variety of advanced, metastatic tumors, as evidenced by two newly unveiled studies from Yale Cancer Center. Both are Phase I clinical trials.

The first study involved an investigational antibody drug, known as MPDL3280A and manufactured by Roche Genentech, which was designed to prevent a cancer cell’s overexpressed PD-L1 protein from putting the immune system to sleep. Yale oncologists reported that the efficacy of MPDL3280A was evaluated in 140 patients with locally advanced or metastatic solid tumors who had exhausted other means of therapy. Tumor shrinkage was observed in patients with non-small cell lung cancer, melanoma, kidney cancer, colorectal cancer, and gastric cancer. Overall, 29 out of 140 patients (21 percent) experienced significant tumor shrinkage, and the highest number of responses were in patients with lung cancer and melanoma.

In the second Phase I study, researchers evaluated the safety and efficacy of combining immunotherapy drugs — nivolumab and ipilimumab — in treating advanced melanoma. Each drug had been known to prolong survival or produce durable tumor regressions in some patients when administered individually, but combining them produced superior clinical results, researchers reported, with rapid and deep tumor regressions in many patients. Researchers provided data for 86 patients in this Phase I trial. They report that responses were generally durable, even in patients whose treatment was terminated early.

**Detecting Breast Cancer: 3D Screening reduces Recall Rates**


Tomosynthesis, or 3-dimensional (3-D) mammography, significantly reduced the number of patients being recalled for additional testing after receiving a mammogram, a Yale Cancer Center study has found. Tomosynthesis was observed in patients with non-small cell lung cancer, melanoma, kidney cancer, colorectal cancer, and gastric cancer. Overall, 29 out of 140 patients (21 percent) experienced significant tumor shrinkage, and the highest number of responses were in patients with lung cancer and melanoma.

**Brain-Penetrating Particle Attacks Deadly Cancers**

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Yale scientists have developed a new approach for treating a deadly brain cancer that strikes 15,000 in the United States annually and for which there is no effective long-term therapy. The researchers have shown that the approach extends the lives of laboratory animals and are preparing to seek government approval for a human clinical trial.

The researchers developed a new, ultra-small drug delivery particle that more nimbly navigates brain tissue than do existing options. They also identified and tested an existing FDA-approved drug — a fungicide called dithiazanine iodide (DI) — and found that it can kill the most aggressive tumor-causing cells. The drug-loaded nanoparticles are administered in fluid directly to the brain through a catheter, bypassing the blood-brain barrier. The particles’ tiny size — their diameter is about 70 nanometers — facilitates movement within brain tissue. They release their drug load gradually, offering sustained treatment.

In tests on laboratory rats with human brain cancers, DI-loaded nanoparticles significantly increased median survival to 280 days, researchers report. Maximum median survival time for rats treated with other therapies was 180 days, and with no treatment, survival was 147 days. Tests on pigs established that the new drug-particle combination also diffuses deep into brains of large animals.

The nanoparticles are made of polymers, or strings of repeating molecules. Their size, ability to control release, and means of application help them permeate brain tissues. The scientists believe the particles can be adapted to deliver other drugs and to treat other central nervous system diseases.

**How have surgical options for women with gynecologic cancers changed over the last decade?**

Surgical options have dramatically changed over the last decade. The biggest impact has been the use of laparoscopic robotic surgery, which provides the same surgical outcomes for patients but with very small incisions, less frequent wound infections, shorter hospitalizations, and quicker recovery times.

Laparoscopic robotic surgery is available to women in need of surgery for uterine cancer, for removal of the uterus, tubes, and ovaries. It is also being offered to women with invasive cervical cancer who require a radical hysterectomy. Laparoscopic surgery is currently being evaluated for women with ovarian cancer, to determine whether optimal upfront surgical cytoreduction is possible, or if neoadjuvant chemotherapy should be used.

You were recently given the Lifetime Achievement Award by Yale Cancer Center to celebrate your career. What advice do you give the next generation of gynecologic oncologists in residency training?

The choice of a career in gynecologic oncology has been a wonderful one for me. Gynecologic oncology is one of the very few specialties where one can provide both surgical and medical treatment for patients with cancer. It allows one to develop a special, long-term relationship with their patients and their families, and gives us the opportunity to oversee all of their cancer care. The next generation of gynecologic oncologists should continue this global approach to patient management, as it has been critical to the development of advances in our field for the treatment of women with gynecologic cancers.

**A Life in YC:**

The Pap smear has dramatically changed the incidence of advanced stage cervical cancer. How close are we to seeing an early detection-screening test for ovarian cancer?

Unfortunately early detection for ovarian cancer remains elusive. The measurement of CA 125 levels in blood samples, along with endovaginal ultrasounds, are the mainstay in detecting ovarian cancer but there is no evidence to show that there is significant improvement in early detection using these approaches in women at high-risk for the disease or in the population at large.

You were the first to use neoadjuvant chemotherapy for advanced ovarian cancers. What impact did that have on the field of gynecologic oncology?

While I started using this approach in 1979 for highly selective patients, American medicine has been slower to adopt the use of neoadjuvant chemotherapy for advanced ovarian cancers than our European colleagues. We are now beginning to see a significant increase in the use of this approach in the U.S., which translates typically into shorter operations, less blood loss, less extensive removal of intra-abdominal organs, shorter ICU and hospital stays, and less frequent postoperative readmission rates. Up to 60% of women in major U.S. medical centers are now being treated with neoadjuvant chemotherapy.