Yale scientists have long been at the forefront in the development of new anticancer drugs, notes Barbara Burtness, MD, Professor of Medicine, Disease Aligned Research Team Leader for the Head and Neck Cancers Program, and Co-Director of the Developmental Therapeutics Research Program. She mentions that chemotherapy was first used against cancer in the 1940s by Yale pharmacologists Louis S. Goodman and Alfred Gilman, who altered toxic mustard gas into a chemical agent against lymphoma.

The challenge for Yale’s researchers in developmental therapeutics hasn’t changed. “When you have an exciting new compound or have figured out how to go after a target,” says Dr. Burtness, “how do you turn that into something that can be studied in patients and become clinically useful?”

Yale’s commitment to therapeutic innovations has recently become even stronger, she adds, exemplified by huge investments in leading-edge facilities and the recruitment of outstanding senior and junior scientists. “In the Developmental Therapeutics Program,” says Dr. Burtness, “we have really built out our capacity to do early phase trials. We have great creative pharmacologists who develop the new drugs, and also the clinical expertise to translate that to patients. There’s the new Phase I Clinical Trial Infusion Center, and we have hired a lot of staff to run early phase trials here ourselves.”

She is particularly excited about Yale’s leadership in developing new immunotherapies against solid tumors. “There are FDA drug approvals in head and neck cancer and in lung cancer that come directly out of the activities of our program,“ she says. “There are a number of us in Developmental Therapies who have played pivotal roles in testing immune checkpoint inhibitors in solid tumors.” She describes some highlights:

Scott Gettinger, MD, Associate Professor of Medicine, reported a large dose-finding study about nivolumab, a targeted antibody that blocks PD-L1. Dr. Gettinger’s trial showed that when used against non-small cell lung cancer, a highly deadly form of the disease, the median survival was 10 months. “That was unprecedented,” says Dr. Burtness, “and has led to a randomized trial establishing nivolumab as part of the standard of care in non-small cell lung cancer.”

Roy Herbst, MD, PhD, Ensign Professor of Medicine and Professor of Pharmacology, Chief of Medical Oncology, and Associate Director for Translational Research, then led a landmark trial showing that non-small cell lung cancer expresses immune suppressing ligands called PD-L1, and that an anti-PD-L1 checkpoint inhibitor called pembrolizumab can turn the immune system back on and superior to the chemotherapy. “That was published in The Lancet,” notes Dr. Burtness, “and pembrolizumab has become the new standard.”

Harriet Kluger, MD, Professor of Medicine, mostly treats melanoma; Sarah Goldberg, MD, MPH, Assistant Professor of Medicine, mostly treats lung cancer—but they both noticed something unexpected when their patients were given immunotherapies. From the cancers that had metastasized to the brain responded to the treatment. This led to a clinical trial to study the effects of pembrolizumab on patients with brain metastases.

Then there’s Dr. Burtness herself, whose primary area of research is head and neck cancers. These are notoriously resistant to treatment, and no new drugs have been approved since 2006. But Dr. Burtness sees great promise in immunotherapy. She and Paul Eder, MD, Professor of Medicine, participated in a multi-center trial of pembrolizumab against head and neck cancer in patients who expressed the biomarker PD-L1. Though the overall response rate was modest (19 percent), it represented a striking improvement over previous treatments for this stubborn disease. In August, the FDA approved pembrolizumab for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma, despite being treated with platinum containing chemotherapy.

Dr. Burtness is confident that further improvements aren’t far off, probably through combination therapies. For instance, she is excited about a promising phase III trial that she is chairing for head and neck cancer that combines pembrolizumab with chemotherapy, in comparison to pembrolizumab alone.

“The most significant point about these new therapies,” says Dr. Burtness, “is that they prolong life for patients with metastatic and recurrent disease who in the past had relatively little hope.”

Building on Immunotherapy’s Success