Published OnlineFirst July 24, 2014; DOI: 10.1158/2159-8290.CD-NB2014-114

"The apparent durability of clinical activity in nivolumab-treated patients is remarkable," the authors wrote. "The persistence of partial tumor regressions and stable disease following nivolumab discontinuation . . . suggests that PD-1 blockage may reset the immune equilibrium between tumor and host."

Investigators will present and publish the results from CheckMate-066 after fully evaluating the data, BMS says. The company also plans to share results with the FDA. ■

A Plan of Attack for Deadly Cancers

The NCI has released strategic plans for making progress against two of the nation's deadliest cancers—lung and pancreatic cancers.

The plans were developed in response to the Recalcitrant Cancer Research Act, passed by Congress in 2012, which required the NCI to develop a scientific framework for advances against recalcitrant cancers. Although the Act defined recalcitrant cancers as those with 5-year relative survival rates below 50%, it directed the NCI to first issue reports spelling out research priorities for at least two recalcitrant cancers with 5-year survival rates of less than 20% that are estimated to kill at least 30,000 Americans a year. Lung and pancreatic cancers are the only two diseases that meet this more limited definition.

The scientific framework for small cell lung cancer (SCLC) was issued on July 1; a plan to address pancreatic cancer was released in March.

"I highly doubt that without the Recalcitrant Cancer Research Act we would have seen a small cell lung cancer report," says Laurie Fenton Ambrose, president and CEO of the Lung Cancer Alliance, a national nonprofit organization that has advocated for a national research plan and will be working with the NCI on its implementation and oversight.

SCLCs account for about 15% to 20% of all lung cancers, and they tend to spread more quickly and resist treatment compared to other types.

The scientific framework identifies five initiatives that could make an impact against SCLC: new tools for tissue collection and tumor models that represent distinct phases of the disease; genomic profiling of SCLC; new diagnostic tests for people at higher risk of developing the disease; molecular-based therapies; and research into factors that define treatment response or resistance. Ambrose expects that the plan will lead to a renewed focus on SCLC research, especially in the areas it highlights.

The scientific framework for pancreatic cancer focuses on research priorities for pancreatic ductal adenocarcinoma, which accounts for 95% of all pancreatic cancers. Priorities include investigating a link between the disease and diabetes; investigating biomarkers for early surgical intervention; developing immunotherapy approaches; and testing treatment strategies that target mutations in *KRAS*, which are present in 95% of pancreatic ductal adenocarcinomas.

Julie Fleshman, CEO of the Pancreatic Cancer Action Network, a nationwide advocacy group, says that the framework is already leading to new projects and funding opportunities. For example, the NCI has launched a major initiative to target *RAS* mutations, which "could potentially have a great impact on pancreatic cancer," Fleshman says.

The frameworks will also help other funding and advocacy organizations complement the NCI's efforts. The Pancreatic Cancer Action Network, for instance, is launching a fellowship award that will fund a researcher to collaborate with the NCI's *RAS* initiative. ■

Bladder Cancers Respond to EGFR Inhibitors

Muscle-invasive bladder cancer (MIBC) is aggressive, hard to treat, and lethal. Researchers now report they've discovered a subtype of the cancer that is vulnerable to EGFR inhibitors.

Although it accounts for about 30% of cases, MIBC causes most bladder cancer deaths. Even after bladder removal, about half of patients die within 5 years. No new treatments for this form of cancer have reached the clinic in more than 20 years, and the heterogeneity of MIBC has posed an obstacle for researchers.

To sort through this diversity, a team led by François Radvanyi, PhD, of the Institut Curie in Paris, France, analyzed gene expression data from 383 MIBC tumors. The researchers found that about a quarter of the tumors fell into a cohesive group that resembled the basal subtype discovered in breast cancer. Clinical data from the patients showed that these "basal-like" MIBC tumors were more deadly than other MIBC tumors.

The basal-like MIBC tumors also revealed a potential vulnerability: They overexpressed genes in the EGFR pathway, including *EGFR* itself. As the researchers reported in July, the EGFR inhibitor erlotinib (Tarceva) diminished cell proliferation in 9 of 11 MIBC basal-like cell lines, but in only 1 of 11 non–basal-like lines (Sci Transl Med 2014;6:244ra91). The EGFR-targeting antibody cetuximab (Erbitux) also proved effective, particularly in 2 basal-like cell lines where it reduced cell numbers by around 75%.

To test whether erlotinib works *in vivo*, Radvanyi and colleagues implanted MIBC tumors into mice. Erlotinib curbed the growth of basal-like tumors, but the non–basal-like tumors didn't respond. The researchers also tested a chemically induced mouse model whose tumors resemble the basal-like growths. Treatment with erlotinib delayed the appearance of the tumors and increased the animals' survival.

Although previous clinical trials in MIBC patients found that EGFR inhibitors had little effect, Radvanyi notes that these studies included patients with non–basal-like tumors who were unlikely to benefit, which might explain the negative results. The team's findings also suggest excluding patients with RAS-activating mutations, which render tumors insensitive to the drugs. MIBC "can't be treated as one disease anymore," says Radvanyi. "It will be several diseases that are treated separately."

What makes the result compelling is that "it was comprehensive across all three types of tumor models," says James McKiernan, MD, of the Columbia University College of Physicians and Surgeons in New York, NY, who wasn't connected to the study.

If further studies confirm the existence of the basal-like subtype, "it is reasonable . . . to take it to the clinic and see if it works," says Mark

AACR American Association for Cancer Research

CANCER DISCOVERY

A Plan of Attack for Deadly Cancers

Cancer Discovery 2014;4:980. Published OnlineFirst July 24, 2014.