Biden: Progress Made with Cancer Moonshot

Former Vice President Joe Biden on April 3 urged optimism in the fight against cancer despite threats by the current administration to drastically cut funding for biomedical research. Biden delivered his remarks as part of an address on the Cancer Moonshot initiative during the American Association for Cancer Research Annual Meeting 2017 in Washington, DC.

“With Cancer Moonshot, we set out to do two things,” he said. “We wanted to inject the urgency of now into this fight by doing in 5 years what would ordinarily take 10, and to change the culture in order to come up with a new strategy in this fight.”

A major milestone was achieved in December when Congress earmarked an additional $1.8 billion for the Beau Biden Cancer Moonshot as part of the 21st Century Cures Act, noted Biden. However, future progress is threatened by the “draconian cuts” proposed by the Trump administration, including $5.8 billion in NIH funding cuts.

If approved, the budget cuts could have a devastating impact, setting back scientific progress “by 15 years” and putting the odds of getting a grant at “an historic low,” said Biden. “This is no time to undercut progress,” he added, but rather time “to double down” in order to deliver on the promise of science and technology.

However, the passage of the 21st Century Cures Act offers reason for hope, he said. The bill passed with broad bipartisan support, and he noted that a separate bill to rename the Moonshot after Biden’s son Beau, who died in 2015 of a brain tumor, was introduced by Republican Senate Majority Leader Mitch McConnell.

The 21st Century Cures Act is an example of the progress that can be made when political parties work together, said Biden. He urged researchers in the audience to continue to push for greater funding on key initiatives and to help legislators prioritize where to invest to get the “biggest bang for the buck.”

Indoximod Combo Triggers Responses in Melanoma

Adding the investigational IDO-pathway inhibitor indoximod (NewLink Genetics) to checkpoint inhibitor therapy led to partial or complete responses in more than half of patients with advanced melanoma enrolled in a phase II trial. The combination has potential to become an effective treatment strategy for patients whose tumors do not respond to PD-1 inhibitor therapy alone, according to preliminary data presented during the American Association for Cancer Research Annual Meeting 2017 in Washington, DC.

In the ongoing single-arm trial, 94 patients with inoperable advanced melanoma received indoximod plus the PD-1 inhibitor pembrolizumab (Keytruda; Merck). After a median follow-up of 10.5 months, investigators reported an overall response rate (ORR) of 52% among 60 evaluable patients, including six complete and 25 partial responses. The combination was well tolerated, with fatigue, headache, and nausea the most frequent side effects, and no grade 4 or 5 events reported.

“Indoximod is an effective inhibitor of the IDO pathway, a key immunoncology target,” said the study’s lead researcher

Cancer never gives up and never surrenders and that’s why we have to use every discipline to fight it, and we’re starting to do that in a more coordinated way,” said Biden. “We can do more together than we can by working alone.” –Janet Colwell

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suppression, from trials, Zakharia said. The ORR in these patients being excluded to standard treatment and often results has been shown to be less responsive patients with ocular melanoma, which been compared head to head. However, the two regimens have not ORR seen with the indoximod combination. ORR was 33%, much lower than the 52% in patients with advanced melanoma, the trial, which tested pembrolizumab alone, Zakharia added. For pathways may be more effective than PD-1 inhibition alone, Zakharia explained. For this reason, tumors can hijack this pathway to evade immune control.

Instead of inhibiting IDO itself, however, indoximod is a tryptophan mimetic that directly influences antigen-presenting cells, such as dendritic cells and macrophages, relieving their immune-suppressive features triggered by IDO-induced low tryptophan levels. Preliminary data from the trial suggest that blocking both the IDO and PD-1 pathways may be more effective than PD-1 inhibition alone, Zakharia added. For example, in the phase III KEYNOTE-006 trial, which tested pembrolizumab alone in patients with advanced melanoma, the ORR was 33%, much lower than the 52% ORR seen with the indoximod combination. However, the two regimens have not been compared head to head.

Notably, the study included nine patients with ocular melanoma, which has been shown to be less responsive to standard treatment and often results in these patients being excluded from trials, Zakharia said. The ORR with the indoximod–pembrolizumab combination rises to 59% if only patients with cutaneous and nonocular melanomas are included in the analysis.

“If verified, these data suggest that [combining IDO and PD-1 inhibitors] may be a strategy for enhancing the likelihood of benefit in this disease,” said Louis Weiner, MD, director of Georgetown Lombardi Comprehensive Cancer Center in Washington, DC. “It has the potential to be a very important milestone in the development of combinatorial strategies, akin to the combination of multiple checkpoint inhibitors.” —Janet Colwell

Medical Centers Sign On to Single IRB Model

The NIH has taken a major step toward ensuring that all multisite trials funded by the agency, including those involving patients with cancer, no longer have duplicative and often superfluous oversight.

The NIH’s National Center for Advancing Translational Sciences (NCATS) announced last month that all 64 medical research institutions funded through the agency’s flagship Clinical and Translational Science Awards (CTSA) program—a $500 million per year effort to move biomedical discoveries into the clinic—had agreed to a legal structure for ceding reviews of human studies conducted at multiple sites to a single Institutional Review Board (IRB). Nearly 100 other medical centers in the United States have also signed on to NCATS’s SMART IRB initiative. Short for “Streamlined, Multisite, Accelerated Resources for Trials,” the SMART IRB platform is aimed at reducing administrative red tape and ensuring consistency in study plans and consent forms across all sites involved in a study. “Time can be life in this instance, especially in cancer,” says Petra Kauffman, MD, director of both the Division of Clinical Innovation and the Office of Rare Diseases Research at NCATS. “We want to move away from that multiple review process to a single IRB.”

Streamlining IRB oversight isn’t an entirely new idea. For more than 15 years, NCI-funded trials have had the option of going through the agency’s Central Institutional Review Board (CIRB). Initially developed for phase III adult oncology trials, the CIRB has expanded to include pediatric, early-phase, and prevention trials.

The NCI review board has yielded considerable savings, in both time and money, for participating institutions. However, NCI participation has always been voluntary, and investigators of NCI-sponsored trials can choose to go through their own institution’s oversight board instead.

Beginning in September, the NIH is scheduled to enact a policy that all agency-funded multicenter clinical studies will have to abide by one IRB, and smoothing that transition is a task that’s fallen to NCATS (available at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html).

In addition to the SMART IRB platform—which Kaufman describes as something akin to a treaty or general framework—NCATS is also copying the NCI model and offering centralized IRB services of its own for CTSA-funded investigators. Last year, the center funded three Trial Innovation Centers: one at Johns Hopkins and Tufts Universities, one at the University of Utah, and one at Duke University and Vanderbilt University Medical Center. As with the NCI CIRB, researchers can opt to use one of the centers’ IRBs. Alternatively, they can meet the new NIH mandate by picking any other IRB of record to review a particular trial, such as one at an institution participating in that clinical trial, or, for cancer trials, the NCI.

Many cancer researchers applaud the effort to bring ethics reviews for every trial under one umbrella. “When you have a well-designed, well-constructed, multicenter clinical study with a model consent form that’s been carefully crafted, the likelihood that a local IRB makes any substantive changes to either the protocol or the consent form is extremely small,” says Richard Schilsky, MD, chief medical officer of the American Society of Clinical Oncology.
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