NCI to Raise Grant Paylines

On February 4, Norman E. Sharpless, MD, director of the National Cancer Institute (NCI) at the National Institutes of Health, discussed the potential afforded by a $120 million NCI budget increase for FY2021 passed as part of a government-wide appropriations bill in December 2020. In a press release, he focused on raising grant paylines, opportunities for established and early-stage investigators, and NCI's recent "15-by-25" goal for cancer research. This is the second consecutive year in which Congress has approved a targeted increase to support NCI extramural grants. The increases provide additional funding for NCI new and continuing (noncompeting) grants. As a result, NCI has raised its payline for R01 research awards for established and new investigators by 35% since 2019 (from the 8th to the 11th percentile) and for R01s for early-stage investigators from the 14th to the 16th percentile. Continuing (noncompeting) awards are being sustained at 100%. As part of its commitment to developing and supporting researchers in the early stages of their careers, during FY 2021 NCI will continue to convert the highest scoring early-stage investigator R01 applications into R37 Method to Extend Research in Time (MERIT) awards, which can provide an additional 2 y of research funding beyond the initial award period.

The additional funding allows progress toward the goal announced in the NCI Annual Plan and Budget Proposal for FY 2022 to raise the payline for R01 applications by 1 percentile/y to reach the 15th percentile by FY 2025. "As we advance towards the 15th percentile, NCI will also address another important priority, cancer health disparities—the differences in the burden of cancer incidence, prevalence, treatment response, and mortality among different populations," said Sharpless. "Just like you, we are committed to cancer research that benefits the entire nation, including individuals, groups, and communities suffering a greater burden of disease than the overall population." Other updates on grant policies are available on the NCI Division of Extramural Activities website at https://deainfo.nci.nih.gov/grantspolicies/FinalFundLtr.htm.

National Cancer Institute

NIH TOPMed Program Analyzes Diverse Genomes

Researchers supported by the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health, announced on February 10 the publication of a groundbreaking study that analyzed >53,000 whole genomes, primarily from minority populations. The study, which appeared on the same day online ahead of print in *Nature* (2021;590:290–299), included data from participants in NHLBI's TransOmics for Precision Medicine (TOPMed) Program. Among other findings, the current study identified 400 million genetic variants, >78% of which had not been previously described; produced the best quality genotype data available for people with African ancestry, who showed the highest genetic variability of the groups studied; and provided new insights into certain gene variants that adversely affect the metabolism of prescription drugs and for which biologic effects may vary by race and ethnic group. More information on the TOPMed Program is available at: https://www.nhlbi.nih.gov/science/transomics-precision-medicine-topmed-program.

National Heart, Lung, and Blood Institute

NRC Patient Video on Radioactive Drug Therapy

In the last week of January, the Nuclear Regulatory Commission (NRC) announced the release of the video "Staying Safe While Getting Better, Protecting Yourself and Your Loved Ones While Taking Radioactive Drugs." The 4-min educational video provides radiation safety guidance and precautions that patients can follow before, during, and after treatment with radioactive drugs to keep exposure to others as low as reasonably achievable. Principles of distance from others, time from treatment, and special hygiene requirements are explained. NRC staff created the video in response to increasing use of online media by patients and family for information about treatments with radioactive drugs. The video is available at https://youtu.be/1cbWFKqpLW0 and is also posted to the NRC website at https://www.nrc.gov/materials/miau/patient-release.html. Patients can view this video and more educational videos on the SNMMI website at http://www.snmmi.org/Patients/Videos/Content.aspx?ItemNumber=13387.

Nuclear Regulatory Commission
SNMMI

FDA Approves CAR-T Cell Immunotherapeutic Breyanzi

The U.S. Food and Drug Administration (FDA) on February 5 approved Breyanzi (lisocabtagene maraleucel; Juno Therapeutics; Seattle, WA), a cell-based gene therapy to treat adult patients with certain types of large B-cell lymphoma who have not responded to or who have relapsed after at least 2 other types of systemic treatment. Breyanzi, a chimeric antigen receptor-T (CAR-T) cell therapy, is the third gene therapy approved by the FDA for certain types of non-Hodgkin lymphoma, including diffuse large B-cell lymphoma. Breyanzi is not indicated for treatment of patients with primary central nervous system lymphoma.

"Today's approval represents another milestone in the rapidly progressing field of gene therapy by providing an additional treatment option for adults with certain types of cancer affecting the blood, bone marrow, and lymph nodes," said Peter Marks, MD, PhD, director of the FDA Center for Biologics Evaluation and Research. "Gene and cell therapies have evolved from promising concepts to practical cancer treatment regimens."

Each dose of Breyanzi is a customized treatment created using a patient's own T cells, which are collected and genetically modified to include a new gene that facilitates targeting and killing of the lymphoma cells. Once modified, the cells are infused into the patient. The safety and efficacy of Breyanzi were established in a multicenter clinical trial of >250 adults with refractory or relapsed large B-cell lymphoma (*Lancet.* 2020;396 [10254]:839–852). The complete remission rate after treatment was 54%. Because severe side effects include the risk of cytokine-release syndrome and neurologic toxicities, Breyanzi was approved with a risk evaluation and mitigation strategy, which includes elements to assure safe use. To further evaluate the long-term safety, the FDA is also requiring the manufacturer to conduct a postmarketing observational study.

The FDA granted Breyanzi Orphan Drug, Regenerative Medicine Advanced Therapy (RMAT), and Breakthrough Therapy designations. Breyanzi is the first regenerative medicine therapy with RMAT designation to be licensed by the FDA. The Breyanzi application was reviewed using a coordinated, cross-agency approach, including both the Center for Biologics Evaluation and Research and the FDA Oncology Center of Excellence.

U.S. Food and Drug Administration

FROM THE LITERATURE

Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Most selections come from outside the standard canon of nuclear medicine and radiology journals. These briefs are offered as a monthly window on the broad arena of medical and scientific endeavor in which nuclear medicine now plays an essential role. The lines between diagnosis and therapy are sometimes blurred, as radiolabels are increasingly used as adjuncts to therapy and/or as active agents in therapeutic regimens, and these shifting lines are reflected in the briefs presented here. We have also added a small section on noteworthy reviews of the literature.

DaTscan and PD Management in NSDD

Isaacson et al. from the Parkinson's Disease and Movement Disorders Center of Boca Raton (FL) reported on February 1 ahead of print in the *Journal of Parkinson's Disease* on the clinical impact of ^{123}I-ioflupane (DaTscan) SPECT brain imaging ordered for evaluation of nigrostriatal dopaminergic degeneration (NSDD) associated with movement disorders. The study included 201 patients with clinically questionable NSDD, their pre- and postscanning diagnoses, and any changes in management. Overall, DaTscan was abnormal in 58.7%, inconclusive in 3.5%, and normal in the remaining patients. DaTscan imaging changed clinical diagnoses in 39.8% of patients and resulted in medication therapy changes in 70.1%. The authors concluded that DaTscan imaging can be useful in determining the presence of NSDD in several relevant clinical scenarios, including in patients with early subtle symptoms, suboptimal response to levodopa, prominent action tremor, drug-induced parkinsonism, and/or with lower extremity or other less common parkinsonism clinical symptoms. Imaging was also useful in identifying underlying NSDD in patients who had been diagnosed with Parkinson disease 3–5 y previously without clinical progression or development of motor fluctuations.

Journal of Parkinson's Disease

^{177}Lu-PSMA-617 vs Cabazitaxel in MCRPC

In an article published on February 11 ahead of print in the *Lancet*, Hofman and multiple collaborators from the TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group reported on a multicenter randomized phase 2 trial comparing ^{177}Lu–prostate-specific membrane antigen (PSMA)–617 therapy with cabazitaxel treatment in patients with metastatic castration-resistant prostate cancer. The study included individuals from 11 centers in Australia in whom cabazitaxel had been considered the next appropriate standard treatment. All participants underwent ^{68}Ga-PSMA-11 and ^{18}F-FDG PET imaging and were determined eligible for the trial with PSMA-positive disease and no sites of metastatic disease with discordant ^{18}F-FDG–positive and PSMA-negative findings. Participants were randomly assigned to treatment with ^{177}Lu-PSMA-617 (n = 98) or cabazitaxel (n = 85). The primary endpoint was prostate-specific antigen (PSA) response defined by a reduction of at least 50% from baseline. Responses in PSA levels were more frequent in the ^{177}Lu-PSMA-617 group than the cabazitaxel group (65 and 37 responses, respectively). Grade 3–4 adverse events occurred in 32 (33%) ^{177}Lu-PSMA-617 patients and in 45 (53%) in the cabazitaxel group. These and other data from the study led the authors to conclude that ^{177}Lu-PSMA-617 "is a new and effective class of therapy and a potential alternative to cabazitaxel."

Lancet

PSMA PET Post-RT PCa Biochemical Recurrence

Rowe et al. from the National Cancer Institute (Bethesda, MD), Cross Cancer Institute (Edmonton, Canada), the Frederick National Laboratory for Cancer Research (MD), and the Walter Reed National Military Medical Center (Bethesda, MD) reported in the February 10 issue of *Radiation Oncology* on a study using PET and multiparametric MR imaging to identify patterns of failure in a group of patients who received adjuvant or salvage radiation therapy after prostatectomy and later experienced biochemical recurrence.