FDA Approves Pluvicto/Locametz for Metastatic Castration-Resistant Prostate Cancer

On March 23, the U.S. Food and Drug Administration (FDA) announced the approval of Pluvicto (^{177}Lu-vipivotide tetraxetan, referred to previously and in the nuclear medicine literature as ^{177}Lu–prostate-specific membrane antigen–617 [^{177}Lu-PSMA-617]) for treatment of adult patients with PSMA-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen-receptor pathway inhibition and taxane-based chemotherapy. On the same day, the FDA approved Locametz (kit for preparation of ^{68}Ga-gozetotide injection), a PET agent for PSMA-positive lesions, including selection of patients with metastatic prostate cancer for whom ^{177}Lu-vipivotide tetraxetan PSMA-directed therapy is indicated. Locametz is the first radioactive diagnostic agent approved in the United States for patient selection in the use of a radioligand therapeutic agent. Pluvicto is the first FDA-approved targeted radioligand therapy for eligible patients with mCRPC that combines a targeting compound (ligand) with a therapeutic radioisotope. Novartis (Basel, Switzerland) announced on the same day that its radiopharmaceutical company, Advanced Accelerator Applications USA, Inc. (Millburn, NJ), expected to have both Pluvicto and Locametz available to physicians and patients within weeks of the approval.

The FDA granted Priority Review for ^{177}Lu-PSMA-617 in September 2021 based on positive data from the multicenter phase III VISION study (NCT 03511664), which provided the efficacy data on which the current approval was based. The study was a randomized (2:1), multicenter, open-label trial that evaluated ^{177}Lu-PSMA-617 plus best standard of care or best standard of care alone (control arm) in 831 men with progressive, PSMA-positive mCRPC. All patients received a gonadotropin-releasing hormone analog or had prior bilateral orchiectomy. Patients were required to have received at least 1 androgen-receptor pathway inhibitor, and 1 or 2 prior taxane-based chemotherapy regimens. Patients in the treatment arm (n = 551) received 7.4 GBq (200 mCi) Pluvicto every 6 weeks for a total of up to 6 doses plus best standard of care. The remaining 280 patients in the control arm received best standard of care alone. The trial demonstrated a statistically significant improvement in the primary endpoints of overall survival and radiographic progression-free survival. The hazard ratio for overall survival was 0.62 (95% CI: 0.52, 0.74) for comparison of the treatment arm versus the best-standard-of-care-alone arm. Median overall survival was 15.3 months in the treatment arm and 11.3 months in the control arm. Interpretation of the magnitude of the radiographic progression-free survival effect was limited because of the number of early dropouts in the control arm. About a third (30%) of patients with evaluable disease at baseline demonstrated an overall response (per RECIST 1.1) with Pluvicto plus standard of care, compared to only 2% in the control arm. The most common adverse events (all grades) reported in the Pluvicto arm of the study were fatigue (43%), dry mouth (39%), nausea (35%), anemia (32%), decreased appetite (21%), and constipation (20%).

The FDA advised that patients with previously treated mCRPC should be selected for treatment with Pluvicto using Locametz or another approved PSMA-11 imaging agent based on PSMA expression in tumors. PSMA-positive mCRPC was defined as having at least 1 tumor lesion with ^{68}Ga-gozetotide uptake greater than normal liver uptake.

"We are delighted by the FDA approval of this transformational, innovative therapy for men with advanced metastatic castrate-resistant prostate cancer," said SNMMI President Richard L. Wahl, MD, in an SNMMI press release praising the approval. "We are proud of the society members who contributed substantially to this new theranostic paradigm, as well as all of the authors who published articles on this therapy in *The Journal of Nuclear Medicine*."

This work builds on the success of prior radiopharmaceutical therapies such as ^{177}Lu-DOTATATE, which has provided significant clinical benefit to patients with neuroendocrine tumors. SNMMI indicated that it plans to provide guidance and support to physicians and patients as the newly approved agents become more widely available. The society has updated its appropriate use criteria for PSMA PET imaging to include an indication of "Evaluation of eligibility for patients being considered for PSMA-targeted radioligand therapy" (see story, this issue). In addition, resources will be developed to educate patients with mCRPC about the new therapy.

"The FDA approval of ^{177}Lu-PSMA-617 is a testament to what nuclear medicine innovators, working closely with clinical colleagues in the prostate cancer care domains, can accomplish with their unique combination of expertise in basic biology, radiochemistry, physics, and instrumentation," said Wahl. "The development of radiopharmaceutical therapies is advancing rapidly, and we fully expect there will be more to come as they can be so effective and beneficial for patients fighting cancer."

U.S. Food and Drug Administration
SNMMI

Updates to Appropriate Use Criteria for PSMA PET

Thomas A. Hope, MD, University of California, San Francisco, CA; and Hossein Jadvar, MD, PhD, MPH, MBA, University of Southern California, Los Angeles, CA

As an indication of how quickly the field of nuclear medicine is advancing, the Appropriate Use Criteria (AUC) for Prostate-Specific Membrane Antigen (PSMA) PET document has been updated (*1*). This is due to the recent U.S. Food and Drug Administration (FDA) approval of ^{177}Lu-PSMA-617 (Pluvicto, ^{177}Lu-vipivotide tetraxetan; Novartis [Basel, Switzerland]/Advanced Accelerator Applications USA, Inc. [Millburn, NJ]) radiopharmaceutical therapy (RPT). Previously the AUC had scored the indication for a posttreatment prostate-specific antigen (PSA) rise in the metastatic castration-resistant prostate cancer (mCRPC) setting as "may be appropriate." This was because no available PSMA-targeted therapies would benefit from imaging using PSMA PET. With the approval of PSMA RPT, the PSMA PET AUC Working Group has split this indication into 2 distinct indications (see supplemental materials, available at http://ow.ly/ABfv30sh3uO). The first is "Posttreatment PSA rise in the mCRPC setting in a patient not being considered for PSMA-targeted radiopharmaceutical therapy," which was again scored as "may be appropriate," because the clinical value of improved tumor localization in grossly metastatic disease is not clear in patients who are not being considered as candidates for PSMA RPT. The second indication is "Evaluation of eligibility for patients being considered for PSMA-targeted radiopharmaceutical therapy," which was scored as "appropriate" given the availability of a PSMA-targeted therapy.

An important point is that the AUC Working Group agreed that both ^{18}F-DCFPyL (Pylarify, ^{18}F-piflufolastat; Lantheus [Billerica, MA]) and ^{68}Ga-PSMA-11 (Illuccix and Locametz, ^{68}Ga-gozetotide; Telix Pharmaceuticals Ltd. [Melbourne, Australia], and Novartis/AAA, respectively) should be considered equivalent for selection of patients for treatment with ^{177}Lu-PSMA-617. In the prescribing information for ^{177}Lu-PSMA-617, the FDA recommended selection of "patients for treatment using Locametz or an approved PSMA-11 imaging agent based on PSMA expression in tumors." However, given the near equivalency of ^{68}Ga-PSMA-11 and ^{18}F-DCFPyL, either of these radiotracers can be used for patient selection.

Another consideration for patient selection is what cutoff should make a patient eligible. Two randomized trials have evaluated ^{177}Lu-PSMA-617 therapy: the VISION and TheraP trials. Optimal PSMA PET criteria for patient selection are not yet well established. In the VISION trial, eligibility required uptake in disease greater than that in the liver, and no measurable disease with uptake less than that in the liver (*2*). Eligibility in the TheraP study required an SUV $\geq$20 at 1 site of disease, an SUV $\geq$10 at measurable soft tissue sites, and no ^{18}F-FDG–positive PSMA-negative sites of disease (*3*). It should be noted that, in general, the higher the uptake on PSMA PET, the better patients respond to treatment (*4,5*). PSMA PET is not only a prognostic biomarker but was shown to be predictive in the TheraP trial, with patients who had an SUV_{mean} $\geq$10 having a higher likelihood of PSA response compared to chemotherapy (cabazitaxel) (*6*). Although the decision in the VISION trial was binary, uptake may be used to help weigh various treatment options. The debate as to whether ^{18}F-FDG PET/CT should also be used to screen patients prior to PSMA RPT is outside of the scope of the PSMA PET AUC, although ^{18}F-FDG PET may provide additional value in identifying ^{18}F-FDG–positive/PSMA-negative sites of disease (*3*).

PSMA PET plays a significant role in the appropriate selection of patients for PSMA RPT. With the approval and availability of 2 PSMA PET agents, this imaging study should be widely available. Overall, these 2 imaging agents are considered equivalent for patient selection.

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ASNC/SNMMI Radionuclide Authorized User Training Course

The joint American Society of Nuclear Cardiology (ASNC) and SNMMI "80 Hour Radionuclide Authorized User Training Course" was launched on April 12 as a 1-of-a-kind online educational resource for a broad community of radionuclide users. The collaborative project is the result of significant investment of time and energy from subject-matter experts and staff from both professional societies. "This was a more than 2-year cooperative effort directly addressing a genuine need in both the nuclear medicine and nuclear cardiology communities," said Vasken Dilsizian, MD, who, as the 2019–2020 SNMMI president, initiated planning for the course and, with James A. Case, PhD, oversaw its development. "As someone who is closely involved with education of radiology, nuclear medicine, and nuclear cardiology trainees, I've long believed that we're missing a key element in preparing our workforce on some of the basics in radionuclide knowledge and technique," said Dr. Dilsizian. "A partnership between 2 of our leading professional societies, leveraging the expertise of their members and the organizational skills of their experienced staffs, has provided an extraordinarily productive environment for creation of this rich and rigorous new resource."

The course is targeted at nuclear medicine physicians and cardiologists who wish to complete the 80 hours of classroom training required by the U.S. Nuclear Regulatory Commission (NRC) to meet 10 CFR 35.290 training and Agreement State equivalents in basic radionuclide handling techniques for medical use of unsealed byproduct material for imaging and localization studies in order to become Authorized Users (U.S. NRC 10 CFR 35.200). Individuals who complete the course will still need hands-on training in simultaneous clinical work experience in their local nuclear laboratories in the required specified areas as attested to by their Authorized User preceptors. "I am particularly pleased that this course will be available to residents in nuclear medicine and fellows in nuclear cardiology," said Dr. Dilsizian. "As diagnostic, therapeutic, and theranostic applications of radionuclides grow in number and complexity and as the range of approved radiopharmaceuticals expands, we will need more Authorized Users with a solid understanding of the requisite knowledge and the adaptability to build on that knowledge along with changing technologies and novel discoveries." In the future, the course may also be useful for nuclear medicine technologists, especially those who intend to take the Nuclear Cardiology Technologist specialty examination. In addition, the course may be useful for other allied health care professionals, such as radiation safety officers and health physicist specialists.

The online course includes 93 modules of video and slide presentations in 5 sections (see Table 1 for content overview). Each module is divided into 2 or 3 chapters, with quiz questions to assess comprehension on chapter content. Participants may go back to review presentation content and reanswer incorrect questions to meet the required passing score. Those who successfully complete the 80 hours of classroom training will receive a certificate of completion from ASNC/SNMMI, which will be recognized by the NRC and Agreement States as part of their Authorized User training requirements.

TABLE 1
ASNC/SNMMI Radionuclide Authorized User Training Course: Content Overview

Section 1: Radiation Protection and Safe Radioisotope Handling
Regulatory Requirements
Forms of Radiation
Radiation Units
Radiation Protection
Section 2: Physics and Instrumentation
SPECT and Planar Nuclear Imaging: Gamma Cameras
SPECT and Planar Nuclear Imaging: Data Corrections
SPECT and Planar Nuclear Imaging: Tomographic Imaging
SPECT and Planar Nuclear Imaging: Quality Control
PET Imaging: PET Cameras
Dedicated PET and PET/CT Imaging: Tomographic Imaging
PET Imaging: Quality Control
Image Post Processing
Tracer Kinetics
Clinical Optimization of Radiopharmaceutical Dosing
Application of Technology for Radiation Reduction
Other Clinical Applications of Planar, SPECT and PET Imaging: Image Acquisition and Processing
Section 3: Radiochemistry and Radiopharmaceuticals
Managing a Hot Lab
Radionuclide Production and Radiopharmaceuticals
Quality Control of Radiopharmaceutical Production Kits
Section 4: Radiation Biology
Radiation Biology Overview
Radiation Injury, Cell, and Organ Responses
Risk Models, Exposure Limits, Deterministic and Stochastic Effects
Section 5: Nuclear Medicine Mathematics and Statistics
Measuring Radioactive Decay
Shielding Calculations
Mathematics of Imaging
Mathematics of Radioactivity

(*Continued on page 17N*)

SNMMI's Role in the Nuclear Medicine Renaissance

Richard L. Wahl, MD, SNMMI President

Nuclear medicine is undergoing a renaissance, as evidenced by the steady introduction and approval of new radiopharmaceuticals, theranostics, and instrumentation. In the past year alone, we have celebrated the U.S. Food and Drug Administration (FDA) approval of new PSMA-targeted prostate imaging and therapy agents, breakthrough research for FAPI PET/CT, new generic SPECT agents, and great advances in artificial intelligence. SNMMI has been there every step of the way to support the field of nuclear medicine and molecular imaging, promoting quality of practice, research and discovery, outreach, and advocacy, all while helping ensure an adequate workforce pipeline for the future.

SNMMI strives to enhance the practice of nuclear medicine by providing professionals with the resources needed to deliver high-quality care. In light of recent advances in the field, SNMMI released appropriate use criteria for PSMA PET imaging and musculoskeletal infection imaging, as well as new procedure standards to assist in obtaining high-quality examinations while simultaneously controlling costs. In February, SNMMI launched its Radiopharmaceutical Therapy Center of Excellence program, which offers options for site designation, and later this year will begin its pilot program for the Radiopharmaceutical Therapy Registry (RaPTR), which supports ongoing data collection and quality improvement in theranostics. SNMMI's Therapeutics Conference, held in March, was well attended and provided education to practitioners wishing to expand their practices to include radiopharmaceutical therapies, such as ^{177}Lu-PSMA-617.

A key SNMMI focus over the past year has been to encourage research. A new initiative, the "Mars Shot" for molecular imaging, focuses on advancing the research and development of diagnostic and therapeutic nuclear medicine. A dosimetry supplement in *The Journal of Nuclear Medicine* addresses both the rapid progress and challenges in applying patient-specific radiation dosimetry to guide radiopharmaceutical therapies, providing a useful starting point for sites considering implementing dosimetry in their clinical practices or research operations. A therapy toolkit has been developed to assist new sites as they begin research projects. An Artificial Intelligence (AI) Summit was held in March to help drive development of AI tools for nuclear medicine. In addition, the society created and awarded 2 Radiopharmaceutical Therapy Research Fellowships to grow the number of trained investigators in our field.

The society has also been successful in advancing its issues and becoming a valued partner among public policy stakeholders. SNMMI is working hard to encourage legislators and regulators to support and pass the bipartisan Facilitating Innovative Nuclear Diagnostics (FIND) Act, a bill to ensure patient access to nuclear medicine scans (www.snmmmi.org/FindAct). A summit was held in March to educate regulatory representatives about health disparities and barriers to patient access to nuclear medicine procedures. The society has also actively worked to maintain and increase reimbursement for the nuclear medicine community, successfully expanding Centers for Medicare & Medicaid Services coverage for nononcologic PET and ^{18}F-FDG PET for infection and inflammation.

Richard L. Wahl, MD

With so much work being done to advance the field, SNMMI realizes the importance of developing a robust pipeline of professionals qualified to practice in all areas of nuclear medicine and molecular imaging, both now and in the future. In the past year, 3 working groups (focused on physicians, scientists, and technologists) were formed to develop content and curricula on radiopharmaceutical therapies and diagnostic procedures for residents. A dedicated resident, medical student, and program director website was also created with tailored content for each group. The society introduced a new education initiative—the Quality Systems Personnel Training Program—to educate individuals with a pharmacy or chemistry background in the production and release of clinical radiopharmaceuticals. SNMMI also launched a new online Career Center which, as of January 2022, has posted more than 2,500 jobs.

Another component of SNMMI's work is outreach. The society reaches referring physicians through presentations at specialty events, such as the Pediatric Endocrine Society meeting and the San Antonio Breast Cancer Symposium. To connect with patients, SNMMI hosted its annual Patient Education Day, which was attended by 223 participants and has received more than 1,000 on-demand views to date. In-person patient roadshows are scheduled to return in 2022. Two new organizations joined SNMMI's Patient Advisory Board in 2021, bringing the total number of participants to 15. Internationally, SNMMI's Department of Energy Grant Taskforce continues to work closely with the Korle Bu Teaching Hospital in Accra, Ghana, to assist in building its nuclear medicine program.

As always, SNMMI supports nuclear medicine and molecular imaging through its meetings and journals. Held virtually last year, the 2021 Annual Meeting welcomed more than 6,000 participants from more than 60 countries, with an expanded scientific program including 80 continuing education and

scientific sessions, 189 scientific oral presentations, 14 satellite symposia, 1,000 scientific posters, and 115 exhibitors. *The Journal of Nuclear Medicine* continues to promote innovative research and dramatically increased its impact factor last year, now ranking third among all medical imaging journals.

In the fall of 2021 SNMMI kicked off a new consumer-focused public relations initiative to raise awareness about what nuclear medicine is and what it can accomplish. By focusing on consumer broadcast media—print and digital news publications, radio, and TV—SNMMI has been able to reach a broad audience, including patients, referring physicians, legislators, regulators, payers, and other media. After only 6 months, the program has provided content to a potential 1 billion consumers.

SNMMI is stable, financially secure, and ready to lead in a new era of nuclear medicine and molecular imaging. As the nuclear medicine renaissance continues, the society is committed to our members and the patients we serve.

(Continued from page 15N)

"This would not have been possible without the generous volunteer efforts of the more than 40 course leads and section faculty who participated in multiple planning meetings and devoted substantial time in developing and preparing highly specialized material for this unique effort," said Dr. Dilsizian. "Kathleen Flood, ASNC CEO, and Virginia Pappas, CAE, SNMMI CEO, deserve special credit for their willingness to bring together their members and staffs to coordinate these efforts. Dawn Edgerton, MA, ASNC Director of Strategic Projects, was an exceptional organizational leader on the project from start to completion."

The leads for Section 1, Radiation Protection and Safe Radioisotope Handling, are R. Glenn Wells, PhD, and David Wolinsky, MD, with section faculty including Dr. Wells and Brian Abbott, MD; Adam Alessio, PhD; Mouaz Al-Mallah, MD, MSc; Jon Aro, BSc; Stephen A. Bloom, MD; Tyler Bradshaw, MD; James A. Case, PhD; Rami Doukky, MD, MSc, MBA; Dawn Edgerton, MA; Michael King, PhD; Ran Klein, PhD, Elec Eng; Yi-Hwa Liu, MD; April Mann, MBA, CNMT, NCT, RT(N); Frederic J. Mis, PhD, CHP; and William Van Decker, MD.

The second section, on Physics and Instrumentation, is led by Keisha McCall, PhD, and Krishna Patel, MD, MSc, with section faculty including Dr. McCall and Mouaz Al-Mallah, MD, MSc; Ian Armstrong, PhD; James A. Case, PhD; Frederic H. Fahey, DSc; James R. Galt, PhD; Ernest V. Garcia, PhD; Saurabh Malhotra, MD; A. Iain McGhie, MD; Zhihua Qi, PhD; Piotr Slomka, PhD; Brett Sperry, MD; and Stephanie Thorn, PhD.

The third section, on Radiochemistry and Radiopharmaceuticals, is led by Saurabh Malhotra, MD, and Sally Schwarz, RPh, MS, with faculty including Dr. Schwarz and William Crisp, PharmD; Reiko Oyama, RPh, MS; Stephen Moerlein, PharmD; Peggy Squires, BS, CNMT; and William Van Decker, MD.

Section 4, on Radiation Biology, is led by Frederic J. Mis, PhD, CHP, and Ronald G. Schwartz, MD, MS, who serve as section faculty along with Andrew Einstein, MD, PhD.

The fifth section, on Nuclear Medicine Mathematics and Statistics, is led by James A. Case, PhD, and Frederic J. Mis, PhD, CHP, who serve as section faculty along with Maria L. Mackin, CNMT, and Ronald G. Schwartz, MD, MS.

Special recognition is also due to Tina Buehner, PhD, CNMT, for her service on the task force and her contributions to the content of this course. The cost of the course for SNMMI and ASNC members is $400 for cardiology fellows and nuclear medicine residents and $550 for physicians. For nonmembers the cost is $700. To learn more about the course and to enroll, see: https://sites.snmmi.org/SNMMIMAIN/80_Hour_Course/80_Hour_Radionuclide_Authorize_User_Training_Course.aspx or https://www.ASNC.org/80Hour.

American Society of Nuclear Cardiology
SNMMI

Petten HFR Restarts Production

NRG (Petten and Arnhem, The Netherlands) announced on March 17 that its High Flux Reactor (HFR) in Petten had been restarted that morning and reached a power output of 45 MW. "Within 2 wk, the first medical isotopes for nuclear medicine will be delivered to hospitals," said Vinod Ramnandanlal, commercial director for NRG and its project partner PALLAS. "We are pleased that NRG can once again meet the global demand for medical isotopes."

The HFR did not start a scheduled production run on 20 January because of a leak in a test facility water system outside of the reactor core. NRG initiated inspections and preparations to restore the system. This required modifications to the facility and submission of an application for regulatory review and approval. This permit was granted on March 9. Directors and staff at reactors in Europe and the United States changed production schedules and methods during the Petten outage to meet radioisotope supply demands.

"This is extremely good news. Medical isotopes are of enormous importance for many patients," said Andor Glaudemans, MD, PhD, president of the Dutch Association for Nuclear Medicine.

The HFR was commissioned in 1961 to develop nuclear technology for energy generation. Beginning in the 1980s, the reactor was increasingly used for production of medical isotopes, particularly for diagnostic applications. Today >30,000 patients/d are treated with medical isotopes from the HFR.

NRG

FDA Guidances Target Cancer Clinical Trials

On March 1, the U.S. Food and Drug Administration (FDA) issued 3 final guidances for industry related to cancer clinical trials. In a press release, the FDA noted that these guidances "parallel the goals of President Biden's recently announced effort to renew and build upon his 2016 Cancer Moonshot initiative to facilitate continued advancement in cancer prevention, detection, research, and patient care." The goals for this renewed initiative are: to reduce death rates from cancer by at least 50% over the next 25 years, to improve the experience of people and their families living with and surviving cancer, and "to end cancer as we know it today."

"With today's actions the FDA is recommending important principles that involve addressing inequities, targeting the right treatments to the right patients, speeding progress against the most deadly and rare cancers, and learning from the experience of all patients," said Richard Pazdur, MD, director for the FDA's Oncology Center for Excellence. "All of these are tenets of Cancer Moonshot's mission."

The first new finalized guidance, "Inclusion of Older Adults in Cancer Clinical Trials," provides recommendations to sponsors and institutional review boards for including older patients (≥65 y) in clinical trials of drugs for cancer treatment. Enrollment of older adults in early-phase cancer clinical trials is recommended, as appropriate, to better inform later-phase studies. Also included are recommendations for trial design, recruitment strategies, information collection, and developing and reporting on more precisely defined older age groups to encourage trial enrollment of this historically excluded population. This guidance is available at: https://public-inspection.federalregister.gov/2022-04399.pdf.

The second new guidance for industry is "Expansion Cohorts: Use in First-in-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics." Advice is provided on designing and conducting trials with multiple expansion cohorts that allow for concurrent accrual of patients into different cohorts to assess safety, pharmacokinetics, and antitumor activity of first-in-human cancer drugs. Pharmaceutical companies and researchers can use trials with expansion cohort designs to assess different aspects of a drug in a single clinical trial to expedite efficient clinical development of the drug. This guidance is available at: https://public-inspection.federalregister.gov/2022-04397.pdf.

The new guidance on "Master Protocols: Efficient Clinical Trial Design Strategies to Expedite Development of Oncology Drugs and Biologics" addresses master protocol design, including information on what sponsors should submit to the FDA as part of these trial approaches. It also directs sponsors on interactions with the FDA to facilitate efficient review and mitigate risks to patients. These clinical trials can expedite clinical development of a drug by allowing more than 1 investigational drug or biologic, more than 1 disease type, or more than 1 patient population to be evaluated under a single clinical trial structure. This guidance is available at: https://public-inspection.federalregister.gov/2022-04398.pdf.

All FDA Oncology Center of Excellence documents are available through the portal at: https://www.fda.gov/about-fda/oncology-center-excellence/oncology-center-excellence-guidance-documents.

U.S. Food and Drug Administration

NCI and Molecular Characterization of Childhood Cancers

The National Cancer Institute (NCI) announced on March 21 the launch of the Molecular Characterization Initiative for pediatric tumors. The program, hosted by NCI's Childhood Cancer Data Initiative, offers tumor molecular characterization (biomarker testing) to children, adolescents, and young adults with newly diagnosed central nervous system tumors who are being treated at hospitals affiliated with the Children's Oncology Group (COG). This NCI-supported clinical trials group includes more than 200 hospitals and institutions treating children diagnosed with cancer in the United States.

Participants with central nervous system cancers will be eligible to receive molecular characterization of their tumors free of charge through this voluntary program. DNA and RNA from tumor and blood samples will be analyzed,

and, later in 2022, the program will be expanded to include soft tissue sarcomas and other rare tumors.

"The ultimate dream has really been for every child with cancer to have a state-of-the-art diagnosis and the safest and most effective therapy," said Brigitte C. Widemann, MD, special advisor to the NCI director for childhood cancer. "The Molecular Characterization Initiative is a transformative collaboration that will entail participation of the entire community."

Comprehensive tumor molecular characterization has previously been available to children enrolling in some clinical trials or being treated at larger institutions with internal resources that offer such state-of-the-art diagnostics. Data on tumor biomarkers have been stored exclusively at the hospital or institution at which a child was treated, with limited data sharing among institutions. The new program will make tumor molecular characterization broadly available, with data collected in a central location accessible to researchers.

"We can help make molecular characterization available throughout the country so that it will be a standard of care that every child can get," said Maryam Fouladi, MD, leader of the COG central nervous system tumor disease committee. "An accurate molecular diagnosis can inform optimal treatment for every child."

In addition to providing detailed information to use in making an accurate diagnosis, the data can also be used to determine whether a child is eligible for a clinical trial. Enrollment in the Molecular Characterization Initiative is initially offered through participation in Project Every Child (http://www.projecteverychild.org/), a childhood cancer registry maintained by COG. Initial participants will include newly diagnosed children, adolescents, and young adults ≤25 y old at the time of diagnoses. Young adults >25 y old who are being screened for eligibility into a COG clinical trial may also be included. Additional information on the initiative is available at: https://www.cancer.gov/research/areas/childhood/childhood-cancer-data-initiative/molecular-characterization.

National Cancer Institute

NIH All of Us Research Program Releases 100,000 Whole-Genome Sequences

The National Institutes of Health (NIH) announced on March 17 the release of nearly 100,000 diverse whole-genome sequences through its All of Us Research Program. About 50% of the data is from individuals who identify with racial or ethnic groups that have historically been underrepresented in research. These data will enable researchers to address new questions about health, disease, and disparities.

"Until now, over 90% of participants from large genomics studies have been of European descent. The lack of diversity in research has hindered scientific discovery," said Josh Denny, MD, chief executive officer of the All of Us Research Program. "All of Us participants are leading the way toward more equitable representation in medical research through their involvement. And this is just the beginning. Over time, as we expand our data and add new tools, this dataset will become an indispensable resource for health research."

The genomic data are available via a cloud-based workbench platform (https://www.researchallofus.org/) and also include genotyping arrays from 165,000 participants. Whole-genome sequencing provides information about almost all of an individual's genetic makeup, whereas genotyping arrays, the more commonly used genetic testing approach, capture a specific subset of the genome.

In addition to the genomic data, the All of Us workbench contains information from many of the participants' electronic health records, Fitbit devices, and survey responses. The platform also links to data from the Census Bureau's American Community Survey to provide more details about the communities in which participants live. This combination of data will allow researchers to better understand how genes can cause or influence diseases in the context of other health determinants. The ultimate goal is to enable more precise approaches to health care for all populations. To protect participants' privacy, the program has removed all direct identifiers from the data and upholds strict requirements for researchers seeking access.

In a press release, NIH noted that these data are made available for research through the contributions of All of Us participants, who have the opportunity to receive personal DNA results at no cost. The program has offered genetic ancestry and trait results to more than 100,000 participants so far, with plans underway to begin to share health-related DNA results on hereditary disease risk and medication–gene interactions later this year. All of Us works with a consortium of partners across the United States to engage participants and collect data and samples. The Researcher Workbench is managed by Vanderbilt University Medical Center, in collaboration with the Broad Institute of MIT and Harvard and Verily. The program's genome centers generate the genomic data and process about 5,000 participant samples each week. These centers include Baylor College of Medicine, Johns Hopkins University, the Broad Institute, the Northwest Genomics Center at the University of Washington, and partners. Color, a health technology company, works with the program to return personalized results to participants on genetic ancestry and traits and the forthcoming health-related genetic results.

National Institutes of Health

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 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.

Radiation Dose to NM Techs from PET/MR and PET/CT

Soret et al. from the Hôpital Universitaire Pitié Salpêtrière (Paris, France) reported on March 16 ahead of print in the *Journal of Radiological Protection* on a study comparing nuclear medicine technologists' radiation doses when performing routine PET/MR and PET/CT acquisitions in the same department. Over 13 mo, daily radiation doses received by technologists were collected with electronic personal dosimeters. Factors included in the retrospective analyses were the total numbers of PET/MR and PET/CT acquisitions, type of study (brain or whole-body PET), ^{18}F-FDG injected activity per day and per patient, and time spent with patients after injection. The researchers found that technologists' whole-body exposure for PET/MR averaged 10.3 ± 3.5 nSv per MBq injected ^{18}F-labeled tracer, compared to only 4.7 ± 1.2 nSv per MBq injected for PET/CT. The additional exposure with PET/MR was attributed to additional time spent in patient positioning and MR coil placement, particularly in whole-body studies. They concluded that "for an equal injected activity, PET technologist radiation exposure for PET/MR was 2-fold that of PET/CT. To minimize radiation dose to staff, efforts should be made to optimize patient positioning, even in departments with extensive PET/CT experience."

Journal of Radiological Protection

Monoclonal Antibodies in Alzheimer Disease

In a study published on March 5 ahead of print in the *Journal of Alzheimer's Disease*, Lacorte et al. from the Italian National Institute of Health (Rome), Sapienza University (Rome), Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico (Milan), and the Casa Cura Policlinico (Milan, all in Italy) provided a systematic review and metaanalysis of published and unpublished clinical trials on the safety and efficacy of monoclonal-based antibody therapies in Alzheimer disease (AD). After a systematized search of clinical trial and literature databases, 101 studies were identified, using a total of 27 monoclonal antibodies. Trial results were available on 50 of these investigations (18 with data from published and unpublished sources, 21 with data from published sources only, and 11 with only unpublished data) using a total of 12 monoclonal antibodies. Assessment of reported amyloid-related imaging abnormalities (ARIAs) in these studies showed overall risk ratios of 10.65 for ARIA-E (MR signal alterations thought to represent vasogenic edema and related extravasated fluid phenomena) and 1.75 for ARIA-H (MR signal alterations attributable to microhemorrhages and hemosiderosis). Metaanalyses of PET SUV ratios indicated an overall significant effect of monoclonal antibodies in reducing amyloid burden. Although data from administration of Clinical Dementia Rating Scale–Sorting Box evaluations showed statistically significant lower rates of worsening in treated patients, these were "clinically nonrelevant." The authors concluded that these results suggested that the risks/benefits of monoclonal antibodies remain unclear. They advised that "research should focus on clarifying the effect of amyloid on cognitive decline, providing data on treatment response rate, and accounting for minimal clinically important differences." In addition, research should investigate the possible long-term impact of ARIA events, including potential predictors of onset.

Journal of Alzheimer's Disease

CTA vs SPECT/CT V/Q in Pulmonary Embolism

Martins et al. from the University of Campinas (Brazil) reported on February 27 ahead of print in *Perfusion* on a direct comparison of multidetector CT angiography (CTA) and ventilation/perfusion (V/Q) SPECT/CT in detection of acute pulmonary emboli (PE) in routine practice. The study included 28 patients (15 men, 13 women; median age, 51.5 y) with suspected acute PE who underwent both imaging procedures. The median duration of symptoms from onset to imaging was 4 d (range, 1–14 d), with a median Wells score of 3.5 (range, 1.5–6). Final diagnoses were determined by clinician consensus (general radiologists and/or nuclear medicine physicians) and supporting clinical, laboratory, and follow-up data. The sensitivity, specificity, positive and negative predictive values, and accuracy for SPECT/CT V/Q in identifying PEs were 84.6%, 80.0%, 78.6%, 85.7%, and 82.1%, respectively. For CTA, the corresponding percentages were 46.1%, 100%, 100%, 68.2%, and 75.0%, with overall agreement between the methods at 57.1%. Ten of the 22 patients with negative CTA findings were positive on SPECT/CT V/Q, and 7 of these were determined to be true-positives. The authors concluded that these results suggested that SPECT/CT V/Q "is more sensitive and accurate than CTA when interpreted by general radiologists and nuclear medicine physicians."

Perfusion

Thyroidectomy Without ^{131}I in DTC

In an article published on March 10 in the *New England Journal of Medicine* (2022;386[10]:923–932) Leboulleux and

a consortium of nuclear medicine, endocrinology, and thyroid cancer experts from throughout France reported on a study using results from a prospective phase 3 trial to compare radioiodine therapy (1.1 GBq ^{131}I after injections of recombinant human thyrotropin) with no radioiodine therapy in patients with low-risk differentiated thyroid cancer after thyroidectomy. The primary objective was to determine whether, in the 2 randomly assigned groups of patients, no radioiodine therapy was "noninferior" to radioiodine therapy, taking into account functional, structural, and biologic abnormalities at 3 y. Noninferiority was defined as between-group differences of <5 percentage points in the presence of abnormal foci of ^{131}I uptake on whole-body imaging that required subsequent treatment (in the radioiodine group only), abnormal findings on neck ultrasound, or elevated levels of thyroglobulin or thyroglobulin antibodies. The researchers also looked at molecular characterization and prognostic factors. The trial included 730 patients (mean age, 52 y; 606 women, 124 men; 367 in the no-radioiodine group and 363 in the radioiodine group) with tumors ≤ 2 cm in diameter. At 3-y follow-up, the percentages of patients in the no-radioiodine group without an event was 95.6%. The corresponding percentage in the group that received radioiodine therapy was 95.9%. Documented events in both groups included structural or functional abnormalities in 8 patients and biologic abnormalities in 23 patients. Events were found to be more frequent in patients with postoperative serum thyroglobulin levels >1 ng/mL during thyroid hormone treatment. No differences in molecular alterations were noted in the 2 groups, and no treatment-related adverse events were reported. The authors concluded that "in patients with low-risk thyroid cancer undergoing thyroidectomy, a follow-up strategy that did not involve the use of radioiodine was noninferior to an ablation strategy with radioiodine regarding the occurrence of functional, structural, and biologic events at 3 years." The article received wide coverage in the public media and professional literature. In a commentary accompanying the article (*N Engl J Med.* 2022;386[10]:990–991), David S. Cooper, MD (Johns Hopkins University School of Medicine, Baltimore, MD) praised the study's focus and noted that other trial results may soon provide additional data on this subject, adding "it is noteworthy that although radioiodine therapy for differentiated thyroid cancer was introduced in the 1940s and 1950s, we will finally have definitive evidence to enable clinicians to maximize its benefits and minimize its risks."

New England Journal of Medicine

Dynamic SLN Biopsy Technique in Penile Cancer

O'Brien et al. from the Peter MacCallum Cancer Centre, the Royal Melbourne Hospital, the Young Urology Researchers Organisation, MURAC Health, and the EJ Whitten Prostate Cancer Research Centre at Epworth Healthcare (all in Melbourne, Australia) presented on March 11 ahead of print in *Urology* a narrated video of an operative standard for dynamic sentinel lymph node biopsy (DSLNB) in penile cancer and a retrospective clinical analysis and discussion of the accuracy of this approach. The study included 64 patients (127 groins) who underwent DSLNB for inguinal lymph node staging of histologically proven penile squamous cell carcinoma. Data analyzed included primary tumor histology, DSLNB pathology, progression to radical inguinal lymph node dissection (RILND), and recurrence patterns. Of the total 64 patients, 53 (82.8%) underwent penile-sparing surgery. Tumor histology in 56 (88%) patients showed pT1–pT2 disease. Of the total 127 groins explored with DSLNB, 19 were positive for malignancy and 108 were negative. Over a mean follow-up of 29 mo, 36 groins progressed to RILND. Only 2 previously negative DSLNB findings were positive on RILND (1 in the groin, 1 in the pelvis). DSLNB was found to have a false-negative rate of 1.9% and a sensitivity of 90.5%, allowing 71.7% of groins to proceed for surveillance instead of prophylactic RILND. The authors concluded that "DSLNB is a safe and accurate method for assessing inguinal lymphadenopathy in men with intermediate- to high-risk penile squamous cell carcinoma and impalpable groins." Their video study was intended to establish an operative standard in this setting consistent with international guidelines and expectations. They added that "standardized use of DSLNB by an experienced team will reduce morbidity while maintaining oncological safety for men with intermediate- to high-risk penile cancer and cN0 disease."

Urology

In-Transit Metastases in Distal Extremity Rhabdomyosarcoma

In an article published on March 12 ahead of print in the *European Journal of Surgical Oncology,* Terwisscha van Scheltinga et al. from the Princess Máxima Center for Pediatric Oncology (Utrecht, The Netherlands), the University Paris-Saclay/Hôpitaux de Paris (France), University Hospitals Bristol and Weston NHS Foundation Trust (UK), Royal Manchester Children's Hospital (UK), Hospital Universitari Infantil Vall d'Hebron (Barcelona, Spain), University of Bari (Italy), University Hospital of Padua (Italy), Great Ormond Street Hospital (London, UK), Amsterdam UMC/University Amsterdam (The Netherlands), the Royal Marsden Hospital (Sutton, UK), Institut Gustave Roussy (Villejuif, France), University Hospital of Wales (Cardiff, UK), and the University Medical Center Utrecht (The Netherlands) reported on a study evaluating the frequency, staging, and survival of pediatric patients with in-transit metastases in distal extremity rhabdomyosarcoma. In-transit metastases are defined as metastatic lymph nodes or deposits occurring between the primary tumor and proximal draining lymph node basin. The study included 109 patients (median age, 6.2 y; range, 0–21 y) with extremity rhabdomyosarcoma distal to the elbow or knee and enrolled in the European Paediatric Soft Tissue Sarcoma Group RMS 2005 trial between 2005 and 2016.

Thirty-seven patients (34%) had lymph node metastases at diagnosis, and 19 of these had in-transit metastases, most in the lower extremities. In 51 patients who underwent ^{18}F-FDG PET/CT, suspicious lymph nodes were detected in 24 (47%), with 14 of these having in-transit metastases (solitary or in combination with proximal nodes). In the 58 patients not undergoing PET/CT, suspicious lymph nodes were detected in 13 (22%), with in-transit metastases in 5. At a median follow-up of 6.3 y (range, 2–12.5 y), 60 (55%) patients were in first complete remission and 9 (8%) were in remission after relapse. One patient was alive with disease, and 37 (34%) had died (2 patients lost to follow-up). The 5-y event-free survival rates for patients with in-transit metastases, proximal lymph nodes, or combined proximal/in-transit metastases were 88.9%, 21.4%, and 20%, respectively. Corresponding 5-y overall survival rates were 100%, 25.2%, and 15%. The authors summarized their findings that in-transit metastases constituted more than 50% of all lymph node metastases in this group of patients with distal extremity rhabdomyosarcoma and that ^{18}F-FDG PET/CT improved nodal staging by detecting more regional and in-transit metastases. In addition, patients with proximal (axillary or inguinal) lymph node involvement appeared to have worse prognoses. The authors advised that "popliteal and epitrochlear nodes should be considered as true (distal) regional nodes, instead of in-transit metastases," recommending biopsy of these nodes especially in distal extremity rhabdomyosarcoma of the lower limb.

European Journal of Surgical Oncology

Assessing ^{131}I Capsule Activity and Reducing Staff Exposure

Zuhayra et al. from the University Hospital of Schleswig–Holstein (Germany) reported on March 17 in *Physica Medica* (2022;96:157–165) on a method for estimating ^{131}I capsule activity by measuring the dose rate at contact of the delivered lead-closed container carrying the capsules and thereby estimating radiation exposure. This method was compared to that of conventional ^{131}I capsule measurement using a dose calibrator. The dose rate on the surface of the closed lead container was measured at 2 locations and correlated linearly with ^{131}I capsule activity measured in a dose calibrator to create calibrating curves. The hand and whole-body (effective) doses were determined with official dose meters during validation of the proposed method in clinical practice. The determination coefficients of linear calibration curves were >0.9974. The total relative uncertainty for estimating ^{131}I capsule activity with the proposed method was less than ±7.5%. The reduction of the hand dose with the proposed method was 97% of the conventional measurements of the ^{131}I capsules by dose calibrators. The authors summarized their findings that "measuring dose rate on the surface of the closed lead containers enables the ^{131}I capsule activity to be estimated simply, reliably, and with sufficient accuracy" to result in significant reduction of radiation exposure for medical staff.

Physica Medica

^{68}Ga-PSMA-11 PET/CT and ADT Monitoring

In an article published on March 4 in *Cancers (Basel)* (2022;14[5]:1329), Tseng et al. from the New Taipei Municipal TuCheng Hospital, Chang Gung University School of Medicine (Taoyuan), and Linkou Chang Gung Memorial Hospital (Taoyuan, all in Taiwan) reported on a pilot study evaluating ^{68}Ga–prostate-specific membrane antigen–11 (^{68}Ga-PSMA-11) PET/CT findings in patients with advanced or metastatic hormone-naïve prostate cancer after 3 mo of androgen-deprivation therapy. The prospective study included 30 men with untreated stage III or IV disease scheduled to receive therapy for at least 6 mo. Participants underwent ^{68}Ga-PSMA-11 PET/CT imaging before the start of therapy and at 10–14 wk. Response was assessed using a number of factors, including the modified PET Response Criteria in Solid Tumors 1.0, with a subgroup analyzed by International Society of Urological Pathology (ISUP) grade. After 3 mo of treatment, all PET/CT variables indicated significant reductions in disease, showing partial response in 24 patients, complete response in 2, stable disease in 2, and disease progression in 2. In 16 patients with ISUP grade 5, SUV_{max} reduction was less marked, and none reached complete response. The authors concluded that these pilot results indicated that "^{68}Ga-PSMA-11 PET/CT imaging holds promise to monitor treatment response after the first 3 mo of androgen-deprivation therapy."

Cancers (Basel)

PSMA-Guided Mets-Directed Therapy in Oligometastatic PCa

Mazzola et al. from the IRCCS Sacro Cuore Don Calabria Hospital (Verona), the Azienda Ospedaliera Universitaria Careggi (Firenzi), University of Florence, University and Spedali Civili Hospital (Brescia), University of Perugia, Humanitas University (Milan), IRCCS Humanitas Research Hospital (Milan), and the University of Brescia (all in Italy) reported on March 9 ahead of print in *Clinical and Experimental Metastasis* on a multiinstitutional study of prostate-specific membrane antigen (PSMA)–guided metastases-directed radiation therapy in patients with bone oligometastatic prostate cancer. The study included 40 men with 56 bone oligometastases detected by PSMA-based PET and with no concurrent androgen-deprivation therapy. Oligometastatic disease presented as a single lesion in 28 patients, 2 lesions in 9 patients, 3 lesions in 2, and 4 lesions in 1 patient (30.3% spine metastases, 69.7% non-spine metastases). All patients underwent stereotactic body radiation therapy (SBRT) with a median dose of 30 Gy (range, 24–40 Gy) in 3–5 fractions. Over a median follow-up of 22 mo (range, 2–48 mo), 1- and 2-y local control rates were 96.3% and 93.9%, respectively, with corresponding distant progression-free survival rates of 45.3% and 27%. Additional analyses showed that the lower prostate-specific

antigen values after radiation were significantly related to distant progression-free survival. Seven patients were directed to a second radiation course with concurrent androgen-deprivation therapy, and 11 patients with polymetastatic spread received androgen deprivation alone. A lower number of treated oligometastases was correlated with higher androgen-deprivation–free survival rates. The authors concluded that PSMA PET–guided SBRT "resulted in excellent results in terms of clinical outcomes, representing a helpful tool with the aim to delay the start of androgen-deprivation therapy."

Clinical and Experimental Metastasis

Bone Marrow Activation, Metabolic Syndrome, and Early Atherosclerosis

In an article published on March 11 ahead of print in the *European Heart Journal,* Devesa and a consortium of investigators from Madrid (Spain) and New York (NY) reported on a study of the associations between cardiovascular risk factors, bone marrow activation, and subclinical atherosclerosis. The study included 745 apparently healthy individuals (624 men, 121 women; median age, 50.5 y, range, 46.8–53.6 y) from the Progression of Early Subclinical Atherosclerosis study. Participants underwent whole-body vascular ^{18}F-FDG PET/MR imaging. Bone marrow activation (tracer uptake above the median SUV_{max}) was assessed in the lumbar vertebrae (L3–L4), and systemic inflammation was evaluated from circulating biomarkers. Early atherosclerosis was assessed by ^{18}F-FDG uptake in 5 vascular territories, and late atherosclerosis was assessed by fully formed plaques on MR imaging. Men were more likely than women to have bone marrow activation (87.6% and 80.0%, respectively) and to have metabolic syndrome (22.2% and 6.7%, respectively). Bone marrow activation was significantly associated with all metabolic syndrome characteristics, with increased hematopoiesis, and with markers of systemic inflammation, including high-sensitivity C-reactive protein, ferritin, fibrinogen, P-selectin, and vascular cell adhesion molecule-1. In a subgroup of participants with no systemic inflammation, bone marrow activation remained correlated with metabolic syndrome and increased erythropoiesis. The coexistence of bone marrow activation and arterial ^{18}F-FDG uptake on PET was associated with more advanced plaque presence on MR imaging. The authors summarized their findings that in "apparently healthy individuals, bone marrow ^{18}F-FDG uptake is associated with metabolic syndrome and its components, even in the absence of systemic inflammation, and with elevated counts of circulating leucocytes." In addition, bone marrow activation was associated with early atherosclerosis, characterized by high arterial metabolic activity on PET, and appeared to be an early phenomenon in atherosclerosis development.

European Heart Journal

Pediatric Multisystem Inflammatory Syndrome After COVID-19

Astley et al. from the University of Sao Paulo/University of Sao Paulo School of Medicine (Brazil) reported in the March issue of *Physiological Reports* (2022;10[5]:e15201) on a case series of 5 pediatric survivors of multisystem inflammatory syndrome after COVID-19 infection (3 girls, 2 boys; median age, 9; range, 7–18 y). The researchers evaluated the children at a mean follow-up of 1.9 mo (range, 1.3–6.2 mo) with ^{13}N-ammonia PET/CT assessment of myocardial blood flow, standard echocardiography, brachial flow–mediated dilation using Doppler ultrasound, a maximal cardiopulmonary exercise test, and blood markers (C-reactive protein, D-dimer, fibrinogen, and troponin-T). At follow-up, 2 patients showed severe perfusion defects in the left ventricular cavity, suggesting extensive myocardial ischemia (myocardial blood flow <2.0), and 1 showed persistent mild pericardial effusion. Another 2 patients showed endothelial dysfunction. None of the patients had chronic conditions predating their COVID hospitalizations. All patients had findings that indicated impairment in cardiorespiratory and oxidative metabolism during physical exercise with consistently lower than predicted values. The authors summarized their findings that this small-group study suggested that previously healthy pediatric patients had impaired myocardial blood flow, endothelial dysfunction, and lower cardiopulmonary capacity at follow-up after multisystem inflammatory syndrome associated with COVID-19. They added that additional exploration of their assessment techniques might aid in clinical decision making for these patients.

Physiological Reports

PET/CT and Sarcopenia in Elderly Mantle Cell Lymphoma

In an article in the February 23 issue of the *Journal of Clinical Medicine* (2022;11(5):1210), Albano et al. from the ASST Civil Brescia, the University of Brescia, and the ASST Valcamonica Esine (all in Italy) reported on a comparative study of the prognostic roles of ^{18}F-FDG PET/CT and CT-estimated sarcopenia in elderly individuals with mantle cell lymphoma. Fifty-three patients (39 men, 14 women; average age, 72.7 y) were included. All participants underwent PET/CT before and at the end of their institutions' standard chemotherapy regimens. Metabolic response was assessed at end-of-treatment PET/CT using Deauville scores. Sarcopenia was assessed as skeletal muscle index derived from low-dose PET/CT images at the L3 level, with specified cutoffs. Thirty-two (60%) patients were defined as sarcopenic. The 3- and 5-y progression-free survival rates were 29% and 23%, respectively. The corresponding overall survival rates were 43% and 33%. At a median follow-up of 50 mo, disease progression or relapse was documented in 37 patients (70%, average time of 17.2 mo; range, 2–62 mo); 26 of those patients had died. Metabolic response, total metabolic tumor volume, total lesion glycolysis, and sarcopenia were all found to be independent prognostic factors for progression-free survival, although no variable was correlated with overall survival. The authors

concluded that baseline evaluation of CT and PET may help to define sarcopenia in elderly patients with mantle cell lymphoma.

Journal of Clinical Medicine

Apatinib in ^{131}I-Refractory DTC

In an article in the February 23 issue of *Frontiers in Endocrinology (Lausanne)*, Du et al. from Affiliated Cancer Hospital of Zhengzhou University/Henan Cancer Hospital (Zhengzhou, China) and People's Hospital of Changshou District (Chongqing, China) described their experience using apatinib in a group of patients with radioiodine-refractory differentiated thyroid carcinoma (DTC). The study included 47 patients (19 men, 28 women; mean age, 55.8 y; range, 48–68 y) who received 500 mg of apatinib daily for a 4-wk cycle. Participants underwent CT or MR imaging at 4 and 8 wk after initiation of treatment and every 8 wk thereafter. Although no patients achieved complete response, 36 (76.6%) achieved partial response and 8 (17.0%) saw stable disease, respectively. The objective response and disease control rates were 76.6% and 93.6%, respectively. The median progression-free and overall-survival rates were 18 and 59 mo, respectively. Of the 91 adverse events documented, 21 were grade 3 or higher. The authors concluded that apatinib has distinct efficacy in radioiodine-refractory DTC in terms of objective response rates and progression-free and overall survival, with a favorable safety profile.

Frontiers in Endocrinology (Lausanne)

Reviews

Review articles provide an important way to stay up to date on the latest topics and approaches through valuable summaries of pertinent literature. The Newsline editor recommends several general reviews accessioned into the PubMed database in February and March. Roussel et al. from University Hospitals Leuven (Belgium), the San Raffaele Scientific Institute (Milan, Italy), Fox Chase Cancer Center/Temple University Health System (Philadelphia, PA), Radboud University Medical Center (Nijmegen, The Netherlands), University of Texas Southwestern Medical Center (Dallas, TX), the Johns Hopkins University School of Medicine (Baltimore, MD), and the University of Pittsburgh School of Medicine (PA) published "Novel imaging methods for renal mass characterization: A collaborative review" on February 22 ahead of print in *European Urology*. Karapanou et al. from the General Military Hospital of Athens, Evangelismos Athens General Hospital, and Alexandra Hospital Athens University School of Medicine (all in Greece) provided an overview of "Advanced RAI-refractory thyroid cancer: An update on treatment perspectives" on March 1 ahead of print in *Endocrine-Related Cancer*. In an article in the February 25 issue of *Frontiers in Endocrinology (Lausanne),* Morris et al. from the National Institutes of Health Clinical Center (Bethesda, MD) reviewed "Parathyroid imaging: Past, present, and future." Alzghoof et al. from Amsterdam UMC/Vrije Universiteit (The Netherlands) and the University of Turku (Finland) summarized "α-Synuclein radiotracer development and in vivo imaging: Recent advancements and new perspectives" on March 15 ahead of print in *Movement Disorders*. Giovanella et al. from the Imaging Institute of Southern Switzerland/Ente Ospedaliero Cantonale (Bellinzona, Switzerland), the University of Turin (Italy), University Hospital of the European University (Limassol, Cyprus), the University of Messina (Italy), and the University Hospital Center Sestre Milosrdnice (Zagreb, Croatia) reported in the March 1 issue of *Cancers (Basel)* (2022;14[5]:1272) on "Molecular imaging and theragnostics of thyroid cancers."