Journal of the National Comprehensive Cancer Network

NCCN Launches NCCN Congress Webinar Series: Biomarkers 101

Beginning Friday, November 3, 2017, NCCN will host its latest live webinar series—Biomarkers 101. Through the NCCN Congress Webinar Series: Biomarkers 101, esteemed faculty from NCCN Member Institutions provide updates on the latest advances in the use of biomarkers in state-of-the-art care for patients with cancer.

The science and practice of oncology are rapidly evolving based on more complete knowledge of cancer genomes and the specific genetic events that drive cancer. This knowledge, coupled with advances in medicinal chemistry, has ushered in an era of precision oncology. Use of molecular testing followed by therapies tailored to the particular molecular landscape of a patient's disease can allow appropriate therapies to be given to patients who are most likely to benefit, while avoiding unnecessary treatment of patients who are unlikely to benefit. Although the availability of new cancer biomarkers is encouraging for diagnosis, prognosis, and treatment decision-making, determining the clinical usefulness and selection of the appropriate testing methodologies can represent a daunting challenge for practitioners.

With the field of biomarkers rapidly advancing, clinical research directly affects how oncologists manage patients. Keeping up with advances in biomarker testing allows clinicians to offer state-of-the-art care to their patients with cancer and to better identify patients that are appropriate for biomarker-directed clinical trials.

The Biomarkers 101 series includes the following webinars:

- What Are Biomarker Tests and How Are They Approved?
  Friday, November 3, 2017 • 12:30 – 1:30 PM EDT
  Long Phi Le, MD, PhD, Massachusetts General Hospital
- How Is Biomarker Testing Enriching Patient Populations for Clinical Trials & Impacting Drug Development?
  Thursday, November 9, 2017 • 1:30 – 2:30 PM EST
  Ross Camidge, MD, PhD, University of Colorado Cancer Center
- Which Biomarker Test Should I Use?
  Tuesday, December 5, 2017 • 12:00 – 1:00 PM EST
  John D. Pfeifer, MD, PhD, Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine
- Which Disease Sites Have Data on the Clinical Utility of Biomarkers?
  Date & Faculty TBD

To register for Biomarkers 101, visit education.nccn.org/biomarkers.

NCCN Radiation Therapy Compendium is Now Complete, Providing Radiation Treatment Recommendations for All 41 Disease Sites

NCCN has announced the release of the newly-completed NCCN Radiation Therapy Compendium. This comprehensive new addition to NCCN's Library of Compendia includes information designed to support clinical decision-making around the use of radiation therapy (RT) in patients with cancer. The content is based directly on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines), and compiles every reference to RT across the 41 guidelines referencing RT.

"By compiling every recommendation for RT in one place, we've made it significantly easier for specialists in RT to stay up-to-date on the very latest recommendations, regardless of how many different cancer types they treat," said Robert W. Carlson, MD, Chief Executive Officer, NCCN. "This targeted content provides radiation oncologists with the specific, cutting-edge information they need, without forcing them to sift through any ex-

doi: 10.6004/jnccn.2017.0174

traneous information. It's part of our ongoing effort to always provide the most pertinent data on emerging treatment practices in the clearest, most efficient way possible."

The NCCN Radiation Therapy Compendium includes a full complement of radiation therapy recommendations found in the current NCCN Guidelines, including specific treatment modalities such as 2D/3D conformal external-beam RT, intensity-modulated RT, intraoperative RT, stereotactic radiosurgery/stereotactic body RT/stereotactic ablative body RT, image-guided RT, low dose-rate/high dose-rate brachytherapy, radioisotope, and particle therapy.

The NCCN Radiation Therapy Compendium will be updated on a continual basis in conjunction with the library of clinical guidelines.

For more information and to access the NCCN Radiation Therapy Compendium, visit NCCN.org/RTCompendium. The compendium is available free-of-charge through March 2018.

New Patient Guidelines From NCCN Offer Much-Needed Clarity Around a Group of Rare Blood Cancers

Patients with blood cancers known as myeloproliferative neoplasms (MPN) have a new resource to help guide them through diagnosis and treatment, in the form of NCCN's latest addition to the NCCN Guidelines for Patients. This NCCN Guidelines for Patients focuses on the 3 most-prevalent types of MPN: polycythemia vera (PV), essential thrombocythemia (ET), and myelofibrosis (MF), which affect approximately 148,000, 134,000 and 13,000 patients, respectively, in the United States.[1] Funding for these patient guidelines was provided through the NCCN Foundation and the MPN Research Foundation.

"As a physician, I find it makes a difference when patients and caregivers have access to the information they need when making treatment decisions, to complement what they're hearing from me," explained Brady L. Stein, MD, MHS, Robert H. Lurie Comprehensive Cancer Center of Northwestern University. Dr. Stein is a member of the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Panel for MPN. "Sitting in the hematologists' office can be an overwhelming experience. These patient guidelines provide the most comprehensive at-home resource available for people with these rare diseases. They cover everything from basic explanations to complicated decision-making around diagnostic confirmation, supportive care techniques, treatment sequencing, adverse effects, and more."

According to Dr. Stein, it's not uncommon for patients diagnosed with MPN not to understand at first that their condition technically represents a chronic form of blood cancer, or that it can progress. In fact, most patients and caregivers have never even heard of MPN prior to diagnosis.

"When I was first diagnosed with ET, I actually left the office feeling relieved," said Christy Sayre, a patient living with MPN. "It wasn't until my pharmacist explained I had a prescription for a chemotherapy drug, that I really had any idea that I had cancer. I just assumed I'd only be taking a blood thinner. I'm grateful that these patient guidelines are helping me to understand what's going on in my body, and why this chemotherapy is the right treatment path for me."

"Having this free information available online and on their smartphones is particularly important for patients who can't just reach out to a friend or relative who's been through the same experience," said Robert W. Carlson, MD, NCCN Chief Executive Officer. "The goal is not just to make them feel more informed, but also less isolated."

NCCN Guidelines for Patients and NCCN Quick Guide sheets—one-page summaries of key points in the patient guidelines—are written in plain language and include patient-friendly tools, such as suggested questions for doctors, a glossary of terms, and medical illustrations of anatomy, tests, and treatment. They are based on the same clinical

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practice guidelines used by healthcare professionals around the world to determine the best way to treat a person with cancer. Each resource features unbiased expert guidance from the nation's leading cancer centers designed to help people living with cancer understand and discuss their treatment options with their providers.

The NCCN Guidelines for Patients and NCCN Quick Guide sheet for MPN are available to read and download for free online at NCCN.org/patients and via the NCCN Patient Guides for Cancer mobile app. Printed editions can also be ordered from Amazon.com for a small fee.

NCCN Guidelines for Patients and NCCN Quick Guide sheets DO NOT replace the expertise and clinical judgment of the clinician.

Reference

1. Physician Characteristics and Distribution in the U.S., 2010 Edition, 2004 IMV Medical Information Division, 2003 SROA Benchmarking Survey.

NCCN Academy Brings Together Experts to Deliberate Challenges and Opportunities for Patient Access, Collaboration, and Guidelines Development

On July 11, 2017, NCCN hosted its Academy for Excellence and Leadership in Oncology: School of Pharmaceutical & Biotech Business in Philadelphia.

The day's first session, "Ensuring Development and Access to Innovative Therapies," featured the following panelists: Niesha Griffith, MS, RPh, FASHP, Vice President, Cancer Services, West Virginia University Health System; Ohad Oren, MD, Department of Internal Medicine, Hospital of the University of Pennsylvania; Alex Thole, Head of Oncology, Sales & Marketing, Sandoz Biopharmaceuticals; and Patricia Wolfangel, Vice President, Xcenda, AmerisourceBergen.

Dr. Goodman began the module on the topic of formularies and the challenges that facilitators face when making decisions surrounding immunotherapy and combination therapies.

Ms. Griffith said that a lot has changed with formularies. While cost, efficacy, and safety were always considerations, she explained, now centers need to consider whether they will be paid for the drug or, if a patient cannot afford it, if there is support available to them. Moreover, she noted the difficulty in obtaining payer coverage for off-label drug use.

Bringing immunotherapies into the mix is going to be a true challenge for payers, said Dr. Oren. "For conventional therapies, we have decade's worth of experience with the side effect profiles. That's a challenge for the payers as they bring on new immunotherapies—we don't have the data for immunotherapy-related auto-immune toxicities," he said.

"Our pharma colleagues in the room are really looking to define value. What type of evidence do they need to bring you?" Dr. Goodman asked Ms. Wolfangel.

"We have gateways with the 21st Century Cures Act," said Ms. Wolfangel, adding the importance of getting value studies into the hands of the payers in a timely manner.

Dr. Goodman then moved the discussion toward the use of value frameworks in oncology. "At this point, how relevant are they?" he asked the panelists.

"They're in their infancy," said Ms. Griffith. "Value frameworks are something we refer to, but it's not something that we use for decision-making."

"What I see [with value frameworks] is a tremendous effort put forth to develop these responses," said Ms. Wolfangel. "We are on a learning curve, and it's pretty steep, but the level of effort being put into it is tremendous."

Mr. Thole added that the industry has a lot of experience with efficacy and safety, but the challenge is where to include the economics. He added that developers of the value frameworks must be thoughtful about the customer and how they are going to use it.

"I look forward to the future when we can have the value framework in health information technology at the point of care," said Dr. Oren. "NCCN Evidence Blocks do

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a terrific job of truly integrating the important parameters that impact a patient's future," he said.

Moving from value to quality, Dr. Goodman asked the panel to consider quality measurement in oncology.

"In the United States, it's a long time coming. We need to take quality into consideration, but I do not believe it's being used for decision-making today," said Ms. Wolfangel.

Mr. Thole said, "Developing a value-based strategy—although it will take a lot of work—is the best strategy."

Creating a shared-risk model pharmaceutical companies can join is going to require much more active participation from manufacturers, explained Dr. Oren. He added that treatments with truly unique mechanisms of action would translate into superior outcomes for patients.

The panel deliberated about the best approach to defining value for single agents within combination therapies.

"We don't know the outcome versus toxicity of the single agents of a combination therapy," said Dr. Oren. "In the absence of robust literatures, there is no answer…we are not there yet."

Will the introduction of biosimilars to the market create a meaningful impact on cost and patient access, asked Dr. Goodman.

Mr. Thole explained that the introduction of biosimilars has injected a 15% savings into the market. According to Mr. Thole, the FDA spends a lot of time with industry to define the evidence levels necessary for biosimilars. "Most of the work you see started before the agency formalized their guidance. At the same time, we recognize that the agency is a critically important stakeholder, but so are the providers and patients."

"There has to be some patient education around biosimilars," said Ms. Griffith. People do not have a good understanding about the clinical and scientific information that it takes to get a drug approved, she said. "From a patient perspective, when I think about biosimilars, anything that is going to decrease cost is a good thing," she added.

Ms. Griffith also mentioned concern about payers' reactions to biosimilars on the market, noting that her pharmacy will only carry 1 biosimilar agent based on what the payers will reimburse.

Mr. Thole discussed the fact that the biosimilar production process has been happening for decades across different manufacturing sites, explaining that each production site is, essentially, manufacturing a biosimilar to the original. "[We've seen] 375 million days of patient experience across 75 countries with the same outcomes as the originator," he said.

"We are living long on these fabulous therapies," added Ms. Wolfangel. "We also have to think about the longer view." Longer progression-free survival opens patients up to financial toxicity and treatment teams need to be prepared to counsel patients, she explained.

In closing, Dr. Goodman asked the panelists what advice they have for industry to ensure patient access to innovative therapy.

"We have to start preparing for the future," said Ms. Griffith. She shared that the value-based payment model is "here to stay." "My other really important message is that one has to consider the patient."

Looking at long-term innovation, Dr. Oren stated that industry must not only achieve fantastic achievements in remission, but also improve quality of life for patients.

Industry must put the same effort into communicating value as they do communicating evidence-based safety and efficacy, added Mr. Thole.

"If you're in the value space, you're in a good place," said Ms. Wolfangel.

The second module, titled, "Meet the NCCN Guidelines Panel Experts," featured the following panelists: Deborah K. Armstrong, MD, Professor of Oncology, The Sidney Kimmel Comprehensive Cancer Center of Johns Hopkins, and Interim Chair of the NCCN Guidelines Panel for Ovarian Cancer; Patrick Brown, MD, Associate Professor of Oncology, Director, Pediatric Leukemia Program, The Sidney Kimmel Comprehensive

Cancer Center at Johns Hopkins, and Co-Chair of the NCCN Guidelines Panel for Acute Lymphoblastic Leukemia; Joan McClure, MS, Senior Vice President, Clinical Information & Publications, NCCN; and Mary Lou Smith, JD, MBA, Co-Founder, Research Advocacy Network, and member of the NCCN Guidelines Panels for Breast Cancer and Breast Cancer Screening.

Dr. Goodman opened the day's second panel with a discussion about evidence submissions to the NCCN Guidelines and the panel members' expectations.

Dr. Armstrong explained that most of the panel members are practicing at academic institutions, so most of the submissions are not surprises. However, she noted that the Ovarian Cancer Panel prefers that submissions include peer-reviewed publication.

"The gold standard is peer-reviewed clinical trial data for therapeutics," explained Dr. Brown. For a therapeutic agent to be included within the guidelines, he said, it requires FDA approval in some indication, but not necessarily the indication for which it is recommended in the guidelines.

"I look very favorably when a stakeholder submits a well-written summary of the information, but it has to be supported by data…the level of evidence is something we take very seriously," said Dr. Brown.

Ms. McClure explained the levels of evidence used within the NCCN Guidelines, noting that level 2A data is the default.

On the subject of evidence, Ms. Smith noted that data is a challenge within the patient community, as well. Recently, Research Advocacy Network hosted a focus group and a major concern for patients was understanding how clinical trial participants compared with the general patient population. According to Ms. Smith, patients have reached a level of sophistication where they are calling for trials to better reflect their general population.

Dr. Armstrong added that patients are not necessarily interested in "statistically significant" findings typically reported in trial outcomes data, but instead, they are interested in overall survival benefits of a therapy.

"How does this thinking get included in the NCCN Guidelines development process?" Dr. Goodman asked Ms. Smith, who is the longest serving patient advocate on an NCCN Guidelines Panel.

"First of all, you have to have the patient at the table," she answered. Ms. Smith discussed the importance not only of the guidelines development, but insisted that it is imperative to get the word out to the public about specific NCCN Guidelines updates.

"Patients will not make decisions until they see what the guidelines say," said Ms. Smith. "Now we have the patient guidelines, which can include information that are not needed in the [clinical] algorithms."

Drs. Brown and Armstrong discussed the difficulty in making recommendations for patients with recurrent diseases, as well as across different demographics, including age, comorbidities, and prior treatments.

"When the guidelines first came out, we had a statement that, for patients with ≥2 treatments, best supportive care was the care option. But then, in our clinics, we realized that this was not the real-life situation," said Dr. Armstrong. She explained that the typical patient with metastatic disease would receive >3–4 therapies with a good performance status throughout the course of the disease. The guidelines recommendations were changed accordingly, but she explained that the best supportive care should always be an option.

Ms. McClure explained that big data might help in predicting patient performance across different disease and demographic subtypes in the clinical setting. However, she noted that there are inherent biases in how oncologists treat patients with metastatic disease.

Dr. Brown added that specific patient characteristics and variables play a huge role in determining treatment. Such variables include demographics, molecular information about the tumor, molecular information about the patient, and patient fitness, as well as the patient's age—especially in diseases such as acute lymphoblastic leukemia where diagnoses span the full spectrum of age.

"Where does personal judgment and experience weigh in when making recommendations?" asked Dr. Goodman.

"Ultimately the provider's judgment and the patient's wishes are what drive treatment decisions," replied Dr. Brown. "The goal of the guidelines is not to replace judgment and preference…I would say they are decision-support."

"The NCCN Guidelines have a statement in them that they should NOT replace clinical judgment," said Ms. McClure. "When looking at large patient populations, we see that 80%–85% are treated on guideline. That's a reasonable benchmark to look for." Ms. McClure explained that the guidelines cannot pertain to every patient and that there are small subsets of patients for whom the guidelines are not appropriate.

"Where is the role of biomarkers in developing the guidelines?" asked Dr. Goodman.

Dr. Brown explained that there is a necessity for clinical information and trials data for a biomarker to be included in the NCCN Guidelines recommendations, as well as a link to an improved outcome. "There is a page in the guidelines within the Diagnosis and Work Up section that includes biomarker tests recommended to have the complete understanding of a person's disease, he said, noting the added importance of biomarkers in determining prognosis and risk stratification.

Dr. Goodman asked Ms. Smith to discuss her experience as a patient advocate on an NCCN Guidelines Panel. "Can you assure me that if I were to come on as a patient advocate that I would be taken seriously?" he asked.

"Yes," she responded. Ms. Smith explained that patient advocates need to be prepared and know what the treatment recommendations are, as well as connect to the research. "I see my role as bringing the patient experience to the panel. To do that, I help the panel members understand what questions the patients may have. I have been very well-accepted by the other panel members," she said.

In closing, Dr. Goodman asked the panelists to discuss what is most important and unique about the NCCN Guidelines.

The guidelines are credible and open to change, said Ms. Smith.

"Data, data, data," said Ms. McClure. "The more and better the data, the better the outcome is likely to be."

Dr. Brown noted that stakeholders must be transparent as the oncology landscape changes, and encourages outside parties to use the NCCN Guidelines submission process to provide data-driven recommendations to the panels.

Dr. Armstrong echoed her fellow panelists, noting that the NCCN Guidelines are a fluid process, and recommendations can be reconsidered if data improve.

The third panel of the day, "Patient Advocacy Update: Policy, Programs, and Effective Collaboration," featured the following leaders in oncology patient advocacy: Karen R. DeMairo, BA, MHSA, Executive Director, Education & Integration, The Leukemia & Lymphoma Society (LLS); Elaine Grobman, Chief Executive Officer, Susan G. Komen Philadelphia; Marialanna Lee, Senior Director, State Government Affairs, LLS; Katherine Sharpe, MTS, Senior Vice President, Patient and Caregiver Support, American Cancer Society; Kirsten Sloan, Vice President, Public Policy, American Cancer Society Cancer Action Network, Inc.; and Meryl Weinreb, BA, MA, Chair, Education & Public Policy, Susan G. Komen Philadelphia.

Dr. Goodman opened the discussion by asking the panelists to consider the burden of cost on patients with cancer.

"Patients are no longer a captive audience," said Ms. Sharpe. She explained that with outpatient treatment, the cost of treatment quickly grows when co-pays are charged each time a patient walks in the door.

Cost burden has a direct impact on access to care and patient outcomes, said Ms. DeMairo. If a patient cannot afford a co-pay, they may not see the doctor; if the patient cannot afford the medicine, they may not fill their prescriptions, she said. For some patients, she explained, "the bottom line comes down to whether to buy the medications or pay the co-pay or pay the electric bill and buy groceries."

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"All of our organizations have been collaborating on policies that are in the patients' best interests," said Ms. Lee. "The ACA made huge strides in taking cost from an insurmountable barrier to something that patients still have to think about, but there are protections that keep it from being a complete barrier."

Ms. Weinreb explained that the way a drug is administered is becoming another barrier to patient access. Because a large number of therapies in the pipeline are oral, the current reimbursement structure would place them under the pharmacy benefit rather than a patient's medical benefit, she said. With co-pay as high at 30%, pharmacy benefit exposes patients to a greater cost burden, she added.

To combat this issue, there are a number of co-pay programs offered by patient advocacy organizations, Ms. DeMairo said.

Stakeholders have to look beyond cost of care, explained Ms. Grobman. "We've spent years trying to educate the population to get into the doctors' offices earlier so that they don't present at stage III or IV. There are women—thousands of them—who are penalized by where they live," she said. "Those women can't afford to listen. They don't have the transportation. They don't have the babysitters. They don't have the food…We have the best care possible here in the community. We need to get them into the clinic to get that care and get it earlier and keep costs down."

Ms. Sloan explained that there are Medicare/Medicaid patients that cannot use co-pay assistance programs, so their options are lower than others. When ACA was enacted, she said, it set into motion a system to keep costs down, while eliminating life-time maximums. Now, she said, the system is moving away from co-pays to coinsurance, which is percentage-based. "Now, coinsurance for a $100,000 therapy is 20% instead of a $20 co-pay."

Ms. Lee added that this move is happening in employer-sponsored programs, as well.

"We are having the conversation on repeal and replace [of ACA]. Can you start us off by commenting on the impact that would have on the cancer community?" Dr. Goodman asked Ms. Weinreb.

"We really don't know what they're doing at this point," she responded. "A lot of this is a mystery. Clearly everyone is terrified. We know what it was like before ACA, and it was not a good situation." She explained that repealing the essential health benefit would be devastating, especially for patients with cancer and survivors.

Ms. Sloan called on both the patient advocacy groups and industry to work together to help show policymakers how interrelated development, access, and patient outcomes are. "All of us as stakeholders need to help policy makers understand that the protections are critical to ensure that patients get the care and services they need. There is no question that the ACA needed to be improved. We have to work together to make these treatments affordable," she said.

"There is no one entity or one stakeholder group that's going to be the one to carry the burden of reducing cost of care," said Ms. Lee. "We are representing who is at the very heart of the cancer care system…we shouldn't do this without the patients."

Dr. Goodman asked the panelists to describe some of the impactful collaborations their organizations have had with industry.

Ms. Sharpe answered that the American Cancer Society has worked with several pharmaceutical companies on initiatives to better engage and acclimate patients around their care, which have resulted in pilot programs around breast and lung cancers.

Ms. DeMairo described a master trial that LLS has begun for patients with Acute Myeloid Leukemia (AML). For the trial, she said, patients who present in the ER newly diagnosed with AML undergo genomic testing and are then put into one of a number of arms that include drugs from a number of different manufacturers.

Another project, she explained, to reach out to communities and develop relationships with national black churches to raise awareness of multiple myeloma in black men in the United States.

The panel discussed the fact that patients have trouble finding information about available clinical trials.

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"One of the services that LLS offers is a clinical trial search center," said Ms. DeMairo. Presently, she explained, there are 2 nurse navigators who work with newly referred patients, review their medical records, examine financials, and find possible trials for them.

"We have also asked to review consents that the company is putting together for a particular trials," said Ms. DeMairo. She said that it is important to have an advocacy expert review consents, as they are another barrier to access for patients.

"How do you manage relationships with pharma so as not to seem biased?" asked Dr. Goodman.

"Our relationships with pharma are based on advancing our missions," said Ms. Sharpe.

"I have found pharma to be extremely honorable partners," said Ms. Grobman.

In closing, Dr. Goodman asked the panelists, "If you could enact a policy change where you would partner with industry or seek industry to further your organization's mission, what would that one policy change be?"

Ms. DeMairo answered that providing access is key.

Ms. Grobman called for industry to stand with the advocacy communities in the community to reach patients who do not have access or cannot afford access.

"We need to put our best minds together to figure out how to take it to the next level of value," said Ms. Lee.

Ms. Sloan called on industry to keep working on the new innovations. "There is a lot that we have to deliver to make sure that the patient is at the center of the care."

Ms. Weinrab discussed the importance of the oncology medical home model, as well as educating primary care physicians about survivorship issues to ensure that survivors receive quality care long after cancer treatment.

"The solution centers around access," said Ms. Sharpe. "Having a diagnosis is hard enough. Not being able to access the care you need shouldn't happen."