NCCN and Society of Nuclear Medicine Join to Advance Oncology Imaging Research

NCCN and the Society of Nuclear Medicine (SNM) are pleased to announce a collaboration to advance research for cancer imaging and therapies. Specifically, NCCN will work with SNM to qualify imaging sites for upcoming research projects utilizing molecular imaging in clinical trials.

NCCN, through its Oncology Research Program (ORP), obtains funding to support scientifically meritorious clinical trials at the 21 NCCN Member Institutions. These studies evaluate innovative combinations and sequencing regimens, mechanisms of action of specific agents, or drug resistance or explore extended uses for specific agents.

As a new initiative of the ORP, the NCCN Specialized Imaging Research Consortium (SIRC) aims to advance the treatment of patients with cancer through the clinical application of specialized imaging technologies. This is achieved by performing high-quality clinical trials of emerging therapeutics integrated with evidence-based research to guide the use of advanced imaging in clinical cancer care.

To help facilitate the SIRC clinical trials, SNM’s Clinical Trials Network will qualify NCCN Member Institutions to ensure standardization across sites. The qualification process includes scanner validation as well as a review of site personnel, research experience, and infrastructure information. Education and training on specific clinical research, clinical trials methodology, and imaging topics will also be provided.

“We know that historically it has been difficult to use molecular imaging agents in multicenter clinical trials due to a number of factors, including lack of qualified imaging sites and a lack of standardization, among others,” said Dominique Delbeke, MD, SNM president. “SNM’s Clinical Trials Network helps to make this process easier, ensuring high-quality imaging and promoting fast, more cost-effective drug development.”

“As personalized medicine continues to emerge rapidly as a major force in health care, the research questions answered by studies conducted through the SIRC will be invaluable to patients,” said Diane Paul, MS, RN, vice president of the NCCN ORP. “We are pleased to collaborate with SNM as we embrace our mission to improve the quality and effectiveness of care provided to patients with cancer.”

New Therapies for Metastatic Disease Addressed in Updated NCCN Guidelines for Breast Cancer

Women with metastatic breast cancer have expanded treatment options for treating the disease and in the prevention of skeletal-related events as outlined in the recently updated NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Breast Cancer. Robert W. Carlson, MD, of Stanford Comprehensive Cancer Center and chair of the NCCN Guidelines Panel for Breast Cancer, presented these and other notable updates to the NCCN Guidelines at the NCCN 16th Annual Conference in March.

Eribulin (Halaven, Eisai Inc.) was added to the NCCN Guidelines as a preferred single agent option in the treatment of metastatic disease, noted Dr. Carlson. Eribulin received FDA approval for the treatment of metastatic breast cancer in patients who received at least 2 prior chemotherapy regimens for late-stage disease, based on results from a phase III study. The study showed that eribulin provided statistically significant overall survival improvements in patients with metastatic breast cancer previously treated with an anthracycline and a taxane.

“Considering there are limited options for women with metastatic breast cancer who have already received other therapies, this is a noteworthy treatment option that the panel felt was important to incorporate into the guidelines,” said Dr. Carlson.

For patients with breast cancer whose disease has metastasized to their bones, the updated NCCN Guidelines now include denosumab (XGEVA, Amgen) as an option for
the prevention of skeletal-related events, such as fractures and bone pain. Denosumab was approved by the FDA following the results of a study comparing denosumab and zoledronic acid (Zometa, Novartis Oncology) finding denosumab to be at least as efficacious as zoledronic acid in preventing skeletal-related events.

Dr. Carlson emphasized the importance of biomarkers as key predictors of cancer outcomes, particularly in breast cancer.

Three biomarkers have historically been used in breast cancer care: estrogen receptor, progesterone receptor, and HER2. These markers have been a reliable guide for treatment and predictor of breast cancer outcomes; however, several emerging biomarkers, such as the CYP 2D6 genotype to determine tamoxifen (Soltamox, AstraZeneca Pharmaceuticals, LP) efficacy, are also being researched extensively.

“The efficacy of tamoxifen therapy for the treatment of breast cancer varies widely among individuals, which has led to several trials trying to determine whether there is an association between the CYP 2D6 genotype and the effectiveness of tamoxifen in preventing breast cancer recurrence,” said Dr. Carlson.

Dr. Carlson stressed that the NCCN Guidelines Panel feels that the available studies examining CYP 2D6 are inconsistent, therefore the panel does not recommend routine testing for CYP 2D6 genotype.

Continuing to capture public interest and attention, Dr. Carlson reviewed the research and evidence leading to the decision for the NCCN Guidelines Panel to reaffirm its existing recommendation of bevacizumab (Avastin, Genentech/Roche) in combination with paclitaxel (Taxol, Bristol-Myers Squibb Company) as an appropriate therapeutic option for metastatic breast cancer.

The findings in the first large, randomized study of bevacizumab in combination with paclitaxel chemotherapy demonstrated an improvement in disease control and response, but no survival advantage compared with chemotherapy alone, and led to both FDA approval of the combination and the addition of the combination to the NCCN Guidelines. Subsequently, several additional studies have been reported that also demonstrate a small disease control advantage with bevacizumab in combination with chemotherapy, but no survival advantage. On the basis of these studies, the NCCN Guidelines Panel continues to include the combination of bevacizumab and paclitaxel as an option. The panel is less supportive of other chemotherapy agents in combination with bevacizumab.

The panel revised the related footnote, which now states, “Randomized clinical trials in metastatic breast cancer document that the addition of bevacizumab to some first- or second-line chemotherapy agents modestly improves time to progression and response rates but does not improve overall survival. The time to progression impact may vary among cytotoxic agents and appears greatest with bevacizumab in combination with weekly paclitaxel.”

The most recent version of this and all the NCCN Guidelines are available free of charge at NCCN.org. The NCCN Guidelines for Patients: Breast Cancer is available at NCCN.com.

Post-Transplant Lymphoproliferative Disorder Section

Integrated into Updated NCCN Guidelines for NHL

A new guideline detailing diagnosis, workup, and treatment options for posttransplant lymphoproliferative disorder (PTLD), as well as stronger recommendations for therapies in follicular lymphoma, topped the list of highlights in a presentation of the updated NCCN Guidelines for Non-Hodgkin’s Lymphomas (NHL). Andrew D. Zelenetz, MD, PhD, of Memorial Sloan-Kettering Cancer Center and chair of the NCCN Guidelines Panel for NHL, presented the updates at the NCCN 16th Annual Conference in March.
The most significant changes to the updated NCCN Guidelines for NHL are the addition of a new guideline for PTLD and a second for NK/T-cell lymphoma. PTLD is a type of lymphoma that is a life-threatening complication and occurs after a solid organ or hematopoietic stem cell transplantation. The majority of PTLD is of B-cell origin, though T-cell lymphomas and Hodgkin lymphoma can also be present.

“PTLD has emerged as a significant complication of solid organ and allogeneic bone marrow transplantation and one the panel felt was important to address,” said Dr. Zelenetz. “Despite recent advances, it remains a major challenge to define indications for preemptive therapies for PTLD and to integrate novel therapeutic approaches with conventional therapies. The NCCN Guidelines now help to provide a solid framework to assist in diagnosis and treatment decisions.”

Dr. Zelenetz explained that understanding the pathogenesis of PTLD and utilizing early detection strategies, such as serial measurement of EBV-DNA load in peripheral blood samples, have assisted in the identification of high-risk patients.

Pertaining to diagnosis and workup of PTLD, the NCCN Guidelines provide recommendations for tests differentiated as either “essential” or “useful under certain circumstances” to help guide clinicians.

Depending on the PTLD subtype, treatment options in the NCCN Guidelines include the reduction of immunosuppression; if EBV-positive, using antiviral prophylaxis such as gancyclovir (Cytovene, Roche); an anti-CD20 monoclonal antibody such as rituximab (Rituxan, Genentech), or chemoimmunotherapy.

Significant updates were also made to the follicular lymphoma section of the NCCN Guidelines including a category 1 designation for 2 therapies previously given lower-level recommendations by the NCCN Guidelines Panel.

Bendamustine (TREANDA, Cephalon Oncology) plus rituximab is now a category 1 recommendation, from category 2A, as a suggested first-line treatment therapy for follicular lymphoma. Dr. Zelenetz detailed the results of a trial showing that bendamustine plus rituximab significantly improved progression-free survival and complete response rates when compared to standard therapy with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) plus rituximab (CHOP-R) in patients with advanced follicular lymphoma, as well as mantle cell lymphomas.

In addition, post first-remission therapy options for follicular lymphoma including rituximab maintenance and chemotherapy followed by radioimmunotherapy are now category 1 recommendations, from category 2B. Recent studies support this category change showing that progression-free survival is dramatically improved with post-remission therapy (radioimmunotherapy after chemotherapy or rituximab maintenance); however, overall survival suggests that therapy at progression is effective.

Dr. Zelenetz also touched upon the value of PET scans in both the assessment and response evaluation of follicular lymphoma.

FDG-PET is used widely for the staging of lymphoma, but few studies to date have evaluated FDG-PET in follicular lymphoma noted Dr. Zelenetz. However, outcomes from 2 recent trials suggest that FDG-PET imaging can distinguish between patients with indolent and aggressive lymphoma, and that the likelihood of aggressive disease increases in parallel with increases in standardized uptake value measurements.

Lastly, Dr. Zelenetz spoke of recent research suggesting that the prognostic factor of the proliferative index (PI) as determined by quantitative image analysis (QIA) in mantle cell lymphoma is robust. Outcomes data notes that a PI of 30% is a clinically meaningful cut-off and identifies a group of favorable patients with a good outcome.

“This information can be particularly helpful in tailoring the intensity of therapy in future clinical trials,” said Dr. Zelenetz.
NCCN Panel Calls for Higher Standards, Better Ways of Translating Molecular Genetics into Clinical Practice

Recent years have produced an increasing number of tests that use molecular genetics to assess the potential efficacy of cancer therapies in individual patients. An expert panel at the NCCN 16th Annual Conference discussed the challenges created by introducing these new tests, measuring their validity and value, and translating them into clinical practice.

The panel, moderated by Clifford Goodman, PhD, of the Lewin Group, called for higher standards in regulating how and where the tests are done, better data to determine their value and cost-effectiveness, and new approaches to determining their optimal uses for today's patient.

Dr. Goodman challenged the panel to consider the issue of molecular testing from 4 perspectives: regulatory responsibility, evidence that a test "works", translation into everyday practice, and value.

Scott Gottlieb, MD, of the American Enterprise Institute pointed out that molecular tests are currently regulated by how they are marketed, not by claims of what the test does. He supports having the FDA or Clinical Laboratory Improvement Amendments (CLIA), regulate the analytic validity of molecular testing while leaving decisions about clinical validity to the clinical community.

Andrew C. von Eschenbach, MD, formerly of the National Cancer Institute and FDA and currently with Samaritan Health Initiatives, Inc., agreed on the great need to assure that tests are consistent in both claims and results regardless of where they are performed. He conceded that this is not always the case currently.

Louis B. Jacques, MD, from the Centers for Medicare & Medicaid Services, described the field of molecular testing as immature and predicted that it would take some years and additional experience to assess either the true analytic or clinical validity of molecular tests.

Lee N. Newcomer, MD, MHA, from the UnitedHealth Group discussed the challenge of working within a juvenile system, particularly for assessing the quality of the test or its clinical utility. He noted the high percentage of inaccurate or misused tests in some settings and added that the coding system for insurance payments is also outdated.

However, Mark G. Kris, MD, of Memorial Sloan-Kettering Cancer Center, noted that some tests have been proven both valid and useful. When performed properly, for example, the EGFR test in lung cancer can identify patients who have a genetic mutation and the potential to benefit from chemotherapy while sparing those who don't from ineffective therapy.

“It is our job as clinical researchers to provide the data that regulators and payors need to make decisions,” said Dr. Kris.

Michael Kolodziej, MD, from Innovent Oncology, agreed with Dr. Kris, but in his role as a community oncologist sees obstacles to using even established molecular tests in practice. He noted that some tests do not result in treatments that make a clear difference in patient survival, and that obtaining the tissue specimens needed for the tests can be difficult or delayed.

Further, Elizabeth Thompson from Susan G. Komen for the Cure explained that the tests can be confusing from the patient perspective. She said that educated patients are aware of the tests and frequently ask their doctors about them but still have trouble understanding how they apply to their specific situation.

Ultimately, the panel agreed that there was a need for better regulation, more data, and improved methods of making the tests accessible to patients across the spectrum of clinical settings.

“These tests are becoming mechanisms for saving money and improving outcomes for our patients. We need to make sure we have the mechanisms in place to make decisions about what is the right treatment, at the right dose, done for the right reason,” Dr. von Eschenbach summarized.