Research News

Gene Assays Reveal Some Unknown Primary Cancers as RCC

Gene expression profiling and/or immunohisto-chemistry can identify occult renal cell carcinoma (RCC) in a subset of patients diagnosed with carcinoma of unknown primary (CUP), suggesting that these patients could benefit from RCC-specific targeted therapy or immunotherapy, investigators contend.

Of 539 with CUP patients presenting at a single center, a 92-gene reverse transcription polymerase chain reaction molecular cancer classifier assay (MCCA) performed on biopsy specimens identified 24 as having RCC. All patients had clinical characteristics typical of advanced RCC, but none had suspicious renal lesions on computed tomography scans, reported F. Anthony Greco, MD, and John D. Hainsworth, MD, of the Sarah Cannon Cancer Center and Research Institute in Nashville, Tennessee in *Clinical Genitourinary Cancer*. "Although further experience is necessary, these patients responded to RCC-specific therapy in a manner consistent with advanced RCC. These patients are unlikely to benefit from treatment with empiric chemotherapy. The reliable identification of RCC patients within the heterogeneous CUP population is possible using MCCA, and has potentially important therapeutic implications," they wrote.

Neil Osterweil, *Oncology Practice*

Radioactive Agent for Adrenal Tumors

The Food and Drug Administration has approved iobenguane I 131 injection (Azedra) for IV use for the treatment of adults and adolescents aged |≥ 12 years with rare adrenal tumors (pheochromo-cytoma or paraganglioma) that are unresectable, have metastasized, and require systemic therapy. This is the first FDA-approved drug for this use.

Approval is based on a single-arm, open-label clinical trial that included 68 patients. The primary endpoint was the number or patients with a 50% or greater reduction of antihypertensive medications lasting at least 6 months; the secondary endpoint was overall tumor response according to traditional imaging criteria. The primary endpoint was met by 17 patients, and the secondary endpoint was achieved in 15.

The most common severe adverse effects were lymphopenia, neutropenia, thrombocytopenia, fatigue, anemia, increased international normalized ratio, nausea, dizziness, hypertension, and vomiting. Furthermore, because this is a radioactive therapeutic agent, there is a warning about radiation exposure for both patients and family members, a risk that is greatest in pediatric patients. Other warnings and precautions include a risk of myelosuppression, underactive thyroid, elevations in blood pressure, renal failure or kidney injury, and pneumonitis. Myelodysplastic syndrome and acute leukemias were observed in patients who received the radioactive agent, and the magnitude of this risk will continue to be studied, the FDA said.

Christopher Palmer, *Oncology Practice*

Treatment Simulation Could Help Personalize Myeloma Therapy

With the help of gene expression signatures, a simulated treatment learning model identified which patients with multiple myeloma (MM) would benefit most from treatment with bortezomib or lenalidomide, researchers reported in *Nature Communications.* The study included 910 participants across 3 phase 3 trials. In all, 20% had a 100% greater-than-average progression-free survival (PFS) benefit from bortezomib, while 31% had a 200% greater-than-average PFS benefit from lenalidomide, wrote Joske Ubels and colleagues of University Center Utrecht, the Netherlands.

The genetic heterogeneity of cancer and risk of treatment necessitate tools that "predict—at the moment of diagnosis—which patients will benefit most from a certain treatment," the researchers wrote. While gene expression signatures can predict a favorable or adverse prognosis, they do not account for the effect of treatment on survival. "The key idea of simulated treatment learning is that a patient's treatment benefit can be estimated by comparing [his or her] survival to a set of genetically similar patients [who] received the comparator treatment," they noted.

The researchers applied an algorithm called GESTURE to combined data from the TT2 (Total Therapy 2 for Multiple Myeloma), TT3, and HOVON-65/GMMG-HD4 trials. These trials compared bortezomib or lenalidomide with conventional therapies for MM. The model identified

180 patients (20%) for whom bortezomib would produce a 100% greater PFS benefit than in the study population as a whole. Conversely, lenalidomide would produce a 200% greater PFS benefit in 31% of patients.

The simulated treatment learning model "can derive clinically actionable gene expression signatures that enable a more personalized approach to treatment," the researchers concluded. The method requires a large dataset but could be useful for trials that have missed their primary endpoint. The next step is to see if the model makes useful treatment predictions for other cancers. The code needed to train and validate the model is available at github.com/jubels/GESTURE.

Amy Karon, *Oncology Practice*

Symptom Clusters May Identify Cancer Patients at Risk for Hospitalization

Network visualizations—graphic representations of the frequency of individual symptoms and the strength of their co-occurrence with other symptoms—could be used by clinicians in urgent-care settings to determine whether a presenting symptom or cluster of symptoms could be safely managed in the outpatient setting or requires hospitalization, according to Bobby Daly, MD, and colleagues at Memorial Sloan Kettering Cancer Center in New York.

"Uncontrolled symptoms are associated with unplanned acute care. Recognition of the complexity of symptom co-occurrence can drive improved management strategies," the investigators wrote. The report was published in the *Journal of Oncology Practice.*

"Patients who receive chemotherapy have, on average, 1 hospital admission and 2 emergency department visits per year, and 40% to 50% of these stem from symptoms related to their treatment. Acute hospitalizations account for 48% of total cancer expenditures. Considerable regional variation exists, which suggests that these hospitalizations may be avoidable," they wrote.

They identified 23,341 unique patient visits to their center's urgent care department in 2016, and included in their analysis only those patients who had received an IV chemotherapy agent, oral antineoplastic therapy, or immunotherapy within 30 days of presentation. They drew on the electronic health record (EHR) for information about the chief complaint and primary diagnosis for each visit.

"By using EHR data fields for [urgent care center] primary diagnoses and chief complaints, we elicited symptom information and linked it to unplanned acute care. Unplanned acute care is of increasing importance to patients because it disrupts patients' treatment trajectories as well as their lives outside the clinic. Use of the EHR also allowed for granular symptom data, such as a particular site of pain rather than just pain itself, which is absent from traditional sources of patient-reported symptom assessments," Dr. Daly and his colleagues said.

The investigators recommend using data from the EHR in combination with "big data" artificial intelligence techniques to allow early detection of patients at risk for symptom clusters.

Neil Osterweil, *Hematology News*

PET-Driven Chemo Strategy Helps Reduce Toxicity in Hodgkin Lymphoma

Positron emission tomography (PET) performed after 2 cycles of BEACOPP chemotherapy could help identify a subset of advanced-stage Hodgkin lymphoma patients who can receive de-escalated treatment without compromising disease control, results of a phase 3 randomized trial show.

Five-year PFS exceeded 85% not only for patients receiving 6 cycles of escalated BEACOPP, but also for patients who were de-escalated to ABVD chemotherapy based on negative PET results, according to the final analysis of the AHL2011 LYSA study, presented at the annual meeting of the American Society of Clinical Oncology.

"This approach allows us to significantly reduce the treatment-related toxicity in most patients, and provides similar patient outcomes compared to standard BEACOPP escalated treatment," said Olivier Casasnovas, MD, of the University Hospital Le Bocage and Inserm, Dijon, France.

The AHL2011 LYSA study included 823 patients (median age, 30; 63% male) with previously untreated advanced classical Hodgkin lymphoma. All patients received PET at baseline, after cycle 2 of chemotherapy, and again after cycle 4.

Andrew D. Bowser, *Hematology News*