[News * Analysis * Commentary * Controversy]

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Medical Home for Oncology: COA Coordinating Plans to Make It Work

BY LOLA BUTCHER

The Community Oncology Alliance is bringing oncologists, insurance companies, and patients together to develop a new business model for the delivery of cancer care. Originally developed for primary care, the patient-centered medical home is an example of the "value-based" delivery models that payers are demanding. Oncology is getting special attention because of the high costs of cancer care and the widespread belief that, through changes in the way care is delivered and paid for, patients can get better care at a lower cost than insurers are now paying.

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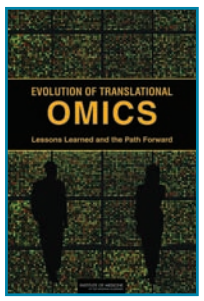
Head and Neck Cancer: New Research Tackles Quality of Life p.16



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Bob Young reviews Otis Brawley's New Book p.38

[ALSO]

PERIODICALS

Meta-Analysis Shows Increased Risk of Death with Anti-VEGF Therapies

BY RABIYA S. TUMA, PHD

SAN FRANCISCO—Many physicians consider molecularly targeted therapies to be relatively benign, but a new meta-analysis shows that isn't always the case. Cancer patients treated with a small molecule inhibitor of the vascular endothelial growth factor (VEGF) receptor had a greater than two-fold relative risk of death due to treatment toxicities compared with patients treated with placebo, researchers reported here at the Genitourinary Cancers Symposium (***Abstract 349***).

"I don't want to scare people," said senior author Toni Choueiri, MD, Director of the Kidney Cancer Center at Dana-Farber Cancer Institute and Assistant Professor of Medicine at Harvard Medical School. "I use these drugs all the time. But the fact is, if these fatal events happen on trials, it means they are happening elsewhere. People are realizing that these drugs are different than cytotoxic drugs, but they are not completely benign overall."

In the current meta-analysis, he and his colleagues identified 10 phase II or III randomized controlled trials that compared FDA-approved (i.e., approved before February 2011) tyrosine kinase inhibitors with placebo in patients being treated for any type of malignancy. Of those, six trials evaluated sunitinib, three tested sorafenib, and one tested pazopanib.

With a total of 4,679 patients included, the team found a 1.5% incidence of fatal adverse events (FAEs) in patients on active drug compared with 0.7% in the placebo arm, for a relative risk of 2.23.

The most common reasons for death were hemorrhage (19 patients, 47.5% of FAEs), myocardial infarction (6 patients, 15%), liver failure (4 patients, 10%), sepsis (3 patients, 7.5%), and congestive heart failure (2 patients, 5%). Additionally, one patient died from each of the following adverse events: ischemic stroke, pulmonary embolism, dehydration, sudden death, and unspecified death. The causes of death are similar to what has been seen in other meta-analyses of individual tyrosine kinase inhibitors, noted first author Christopher J. Richards, MD, of Beth Israel Deaconess Medical Center, who presented the new data.

"Our analysis may underestimate the true incidence of FAEs, as study patients may be healthier than the general population exposed to these drugs," he said, echoing Choueiri's point that if these fatal adverse events are being seen on trials, they will be seen in regular patient care.

TONI CHOUEIRI, MD: "I don't want to scare people. I use these drugs all the time. But the fact is, if these fatal events happen on trials, it means they are happening elsewhere. People are realizing that these drugs are different than cytotoxic drugs, but they are not completely benign overall."

"That being said, all three of the study drugs have been shown in various randomized controlled trials to improve clinical outcomes compared with traditional therapies," Richards continued. "The associated risk of these small molecule tyrosine kinase inhibitors have been demonstrated in this and other studies, but is still incompletely understood."

'Weigh in Context'

The study's Discussant, Thomas E. Hutson, DO, PharmD, Director of the Genitourinary Oncology Program at Baylor Sammons Cancer Center and Co-Chair of Genitourinary Research at US Oncology, emphasized the need to weigh these newly quantified risks in the context of patient benefits. He noted that during the tyrosine kinase inhibitor era, progression-free survival for renal cell cancer patients has improved from two to three months with best supportive care to longer than 11 months with the targeted agents. Overall survival has improved as well, although that has been harder to quantify in clinical trials, he noted.

"I feel confident that everyone, or almost everyone, in the room today would agree with me that our current therapy benefit outweighs the risk associated with treatment."

He also noted that the FDA's Risk Evaluation and Mitigation Strategy (REMS) is aimed at helping to track and limit problems when a risk-benefit equation is not clearly in favor of the drug. Several renal cell cancer therapies have been subject to REMS, including sunitinib and pazopanib, although both have subsequently been released from the program.

Another way to consider risk is to compare the toxicities associated with one accepted therapy with those of another. In that case again, he said, the data favors tyrosine kinase inhibitors. For example, cytonephrectomy surgery trials showed a 2.5% rate for FAEs, and high-dose interleukin-2 had an associated mortality rate of 6% when it was approved, although it has dropped to 0.5% as physicians have improved their protocols and gained experience with the agent.

A 1.5% incidence of FAEs is "certainly in line with other therapies we use for renal cell cancer," he said. "I believe the benefit for targeted therapies exists across all renal cell cancer patients with visible median overall survival improvements…. However, as the authors have noted, there are serious adverse events, including fatal events, that can occur with therapies and therefore, these agents need to be used with caution."

Key Word: Caution

Caution was the point Choueiri emphasized during an interview. He said that despite the name of targeted therapies, it is important that physicians recognize that these drugs do have toxicities, and they should take the time to discuss the risks with patients. Additionally, he said, an individual patient's history needs to be taken into account when prescribing these drugs and deciding on a follow-up schedule.

For example, if a patient has a history of heart disease, the prescribing oncologist should make sure the patient is evaluated and followed by a cardiologist, even if the patient has no current symptoms. "We should see these patients frequently and they should be seen as part of a multidisciplinary care team," Choueiri said.

The full results of the meta-analysis are published in the *Journal of Clinical Oncology* ***(2012;30:871-877).***

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—Study Discussant Thomas E. Hutson, DO, PharmD

Meeting Co-Sponsors

The symposium is co-sponsored by the American Society of Clinical Oncology, the American Society for Radiation Oncology, and the Society of Urologic Oncology.