[News * Analysis * Commentary * Controversy]

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How Harold Freeman Navigated the System to take Patient Navigation from Concept to Standard of Care

BY ERIC T. ROSENTHAL

Patient navigation, conceived more than two decades ago to address disparities in access to health care among the poor and uninsured, will soon become a mainstream medical necessity with the American College of Surgeons Commission on Cancer mandate that cancer centers offer such services by 2015 as a condition for accreditation. Still, there are as yet no specific regulations regarding standardized training. This is part one of our look at the history and evolution of the concept to see how—and if—the cancer community is responding to guide patients through an increasingly complex health care system.

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AACR Capitol Hill Speakers: Keep Cancer Research Funding Strong! p.8

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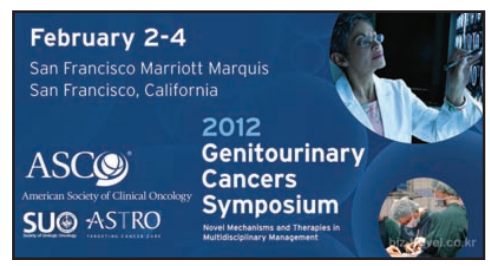

Higher BRCA1/2 Expression Associated with Exercise in Normal Prostate Tissue p.18

[ALSO]

PERIODICALS

ODAC Votes No to Denosumab in High-Risk Men with Castrate-Resistant Prostate Cancer

BY PEGGY EASTMAN

WHITE OAK, MD—The FDA's Oncologic Drugs Advisory Committee voted at a meeting last month not to recommend that denosumab be approved for a new indication—treatment of men with castrate-resistant prostate cancer (CRPC) at high risk of developing bone metastases.

About 54,000 US patients are in that category. The drug is currently approved to prevent skeletal-related events (SREs) in men with CRPC who already have prostate cancer bone metastases. The FDA does not have to take ODAC's recommendations, but often does.

All committee members voted no except for James Kiefert, EdD, the ODAC patient representative, who voted yes on the proposed new indication because he said he and the patients in the support group he runs very much wanted to see oncologists have another tool in their armamentarium to treat high-risk CRPC. "When you become castrate-resistant you have very few options available to you," he said.

RICHARD PAZDUR, MD: "The issue here is that we're not treating a bone scan; we're treating a patient…This is a higher bar that we're talking about."

At issue for the majority of ODAC members was that the data presented by the drug's sponsor, Amgen, Inc., showed a modest 15% reduction in risk for a first bone metastasis-free survival event, and that 74% of bone metastasis events were asymptomatic. There were no demonstrated effects on overall survival, progression-free survival or patient-reported outcomes. Denosumab decreased the time a patient went without developing bone metastasis by a median of 4.2 months.

Despite persuasive vocal testimony for the new indication by physicians in clinical practice and by patient advocates, most ODAC members felt that these relatively modest benefits were not strong enough to offset a greater than 6% per-patient

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"I attended a meeting a few weeks ago of a Michigan organization of medical oncology practices that was an early adopter of the QOPI project, but has taken quality to a new level that I have not seen elsewhere. The catalyst of their success is a partnership with Blue Cross Blue Shield of Michigan."

→SIMONE

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BCBSM is a large, single-state, not-for-profit Blue Cross Blue Shield plan, which had 4.3 million members in 2010. In 2006, BCBSM developed its Value Partnerships program as a hospital, physician, and payer partnership to improve the quality of medical care. The Physician Group Incentive Program (PGIP) is one component of the program. There are currently more than 40 PGIP initiatives in which nearly 15,000 Michigan primary care physicians and specialists representing 40 physician organizations participate.

PGIP initiatives focus on measurable improvements in structure, process, outcomes, and performance; respect physicians' roles as primary owners of the patient care relationship; provide performance rewards to recognize prepared, proactive teams; and reward participants for improvement and collaboration, not just high performance.

BCBSM provides the funding that supports data registries and analysis; administration and incentives for participation and performance; serves as a catalyst for change by uniting providers to improve care throughout the state; and, depending on the initiative, provides clinical advice and expertise to ensure the success of the initiative.

'Truly Visionary'

This is a truly visionary application among health care payers, raising quality and efficiency to the top of the priority list, and not just with formulaic words, but also with action and financial investment.

This support enabled MOCQ to develop a system of quality improvement based on determining the root cause of non-compliance, ranking them by importance and testing new approaches to overcoming that shortfall, using targeted projects for small groups of representative physicians.

"They have moved from measurement to influencing improvement by comparison with tailored interventions, and ultimately will install a rapid learning structure for continuous quality improvement."

In other words, they have moved from measurement to influencing improvement by comparison with tailored interventions. Ultimately, they will install a rapid learning structure for continuous quality improvement. Such a system was described in the *Journal of Clinical Oncology (Abernethy AP, Etheredge LM, Ganz PA, et al. Rapid-learning system for cancer care. **2010; 28:4268-4274***).

Increasing Reimbursement for Care by Oncologists Who Participate in Quality Improvement and Show Progress

BCBSM has pushed the envelope even further by beginning a process of increasing the reimbursement for care by oncologists who participate in quality improvement and show progress in the quality of care.

And the physicians, nurses and office staff have pushed the envelope of their activities further, as well. They have formed the Michigan Breast Oncology Quality Initiative and the Michigan Oncology Clinical Treatment Pathways Program. Detailed analyses are routinely carried out to assess the actual practice patterns and to compare them with accepted standards. This practice is well developed in breast cancer but it is also being examined in other areas. These groups have excellent participation and communication both among and between them.

What is remarkable about these activities is the level of collaboration between many oncology practices large and small, a university cancer program, and a major health care insurer. Even more remarkable is that this group continues to extend its reach in scope and its aspirations for better performance.

The mood at the meeting was exhilarating; a sense of engagement and pride were quite evident. They like doing this because they believe it is the right thing to do. They volunteer their time to make things better organizationally and for their patients.

Although there must be interest in controlling the cost of care, I never heard this discussed substantively by the doctors or by representatives of BCBSM. I believe that they have confidence, as I do, that if you give higher quality of care, the costs will at least rise more slowly and, in some cases, will decline.

For those interested in going beyond the bare minimum of quality improvement, a study of the Michigan model would be the place to start.

→ODAC

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incidence of osteonecrosis of the jaw (ONJ). The risk of ONJ with denosumab is cumulative, so the longer a man with CRPC is on the drug, the higher the risk.

ODAC Chairman Wyndham Wilson, MD, PhD, Chief of the National Cancer Institute's Lymphoma Therapeutics Section in the Metabolism Branch of the Center for Cancer Research, said that when a drug is approved for maintenance or preventive therapy, the magnitude of the drug's benefit for a proposed new indication would have to be higher than what was presented by denosumab's sponsor.

"There's an assumption that delaying bone metastases is beneficial. We are looking at a radiographic benefit here; this is a completely artificial endpoint," he said, noting that the frequent bone scans in the Amgen data (every four months) would be unlikely in a typical practice setting.

"Standard practice isn't looking for bone metastases every four months," Wilson said, adding that if the magnitude of the benefit—a delay in development of bone metastasis—had been six months or longer, rather than four months, he would have felt much more comfortable considering the new indication for denosumab. And, he asked, "By delaying the pattern of bone metastases, are you shifting the disease to another site? It's an interesting biological question."

Trend of More Applications for Proposed Prophylactic or Maintenance Indications

Wilson noted that ODAC is seeing more and more applications for proposed prophylactic or maintenance indications for cancer drugs—which would expose patients for a longer period of time than they would otherwise be exposed to a drug for therapy. So, he said, "We have to be very careful."

Richard Pazdur, MD, the FDA's Director of the Office of Hematology and Oncology New Products, Office of New Drugs, agreed on the need for caution. "The issue here is that we're not treating a bone scan; we're treating a patient…This is a higher bar that we're talking about." In December 2010 ODAC recommended against finasteride and dutasteride for prostate cancer chemoprevention. At that time, Wilson said, "My attitude is, you do no harm."

ODAC temporary voting member Ralph D'Agostino, PhD, Chair of the Mathematics and Statistics Department at Boston University, said that what bothered him was this question: Would giving denosumab early in a castrate-resistant prostate cancer patient's course render the drug less effective or useless later on? He also questioned the significance of the fact that 73% of bone metastases were asymptomatic.

But Roger Dansey, MD, speaking for Amgen Global Development, replied that a percentage of 25% of men with symptomatic bone metastases was "quite significant." The Amgen data presented on behalf of the new drug indication derived primarily from a large randomized, placebo-controlled multicenter Phase III study (known as Trial 147) comparing the treatment effect of denosumab with placebo in prolonging the time high-risk patients with CRPC live without progressing to bone metastases.

The study enrolled 1,432 men with CRPC free of bone metastases at enrollment who had a prostate-specific antigen (PSA) value of 8 ng/mL or greater or a PSA doubling time of 10 or fewer months.

Denosumab principal investigator Matthew R. Smith, MD, PhD, Professor of Medicine at Massachusetts General Hospital Cancer Center, spoke strongly in favor of the new indication for the drug in high-risk patients. "This is not maintenance therapy; these patients have progressive, high-risk disease," he said. "The time without burden of bone metastases is very important to our patients. The endpoint of this trial was very purposeful: to detect bone metastases. This is the appropriate endpoint for a bone-targeted drug."

He also addressed the issue of patients with asymptomatic bone metastases: The idea that high-risk CRPC patients whose cancer has spread to bone would remain asymptomatic for long "is not realistic," he said.

Osteonecrosis of the Jaw

ODAC members discussed ONJ, the most troubling adverse reaction with denosumab (hypocalcemia is the other major side effect) in detail. Dansey said that most of the patients in Trial 147 had mild ONJ, and most already had one or more oral risk factors. "ONJ is manageable today. We have educated oncologists on this," he said, so that they can intervene earlier with a referral to a dentist or oral surgeon when they spot signs of ONJ.

Neal Shore, MD, a community-based urologist who spoke in favor of denosumab during the public portion of the ODAC meeting, said of ONJ, "It's nowhere near as imposing as it seems to be from these discussions." He added that he found it "astounding" that high-risk CRPC patients, especially those with rapid PSA-doubling times, would not want to take denosumab to prevent bone metastases.

Todd Buchanan/ASCO 2012

MATTHEW R. SMITH, MD, PHD: "This is not maintenance therapy; these patients have progressive, high-risk disease. The time without burden of bone metastases is very important to our patients. The endpoint of this trial was very purposeful: to detect bone metastases. This is the appropriate endpoint for a bone-targeted drug." He also addressed the issue of patients with asymptomatic bone metastases, saying that the idea that high-risk CRPC patients whose cancer has spread to bone would remain asymptomatic for long "is not realistic."

Urologist Deepak A. Kapoor, MD, Chairman and CEO of Integrated Medical Professionals, PLLC, a large practice in New York State, also spoke in favor of the proposed new indication. He emphasized that the delay of bone metastases and skeletal-related events is of "paramount importance" to an active older man's ability to live independently.

Kapoor noted that about 50% of men with prostate cancer bone metastases will develop SREs, and he discussed a patient of his who had to start using a wheelchair as a result of compression fractures. For this patient, the result was devastating: he could no longer care for his elderly wife, and she had to go into an extended care setting. "This scenario is becoming more and more common," Kapoor said.

Few African American Patients in Trial 147

The low number of African American participants in Trial 147 (6%) also troubled ODAC members, since prostate cancer has a higher incidence in African American men than in white men. Prostate cancer survivor Thomas Farrington, President and Founder of the Prostate Health Education network, an African American who spoke during the public portion of the ODAC meeting, said the patient community was excited about the evolution in treatments that had led to the proposed new indication for denosumab. African Americans bear an "uneven burden" in prostate cancer, he said, urging ODAC to approve the proposed new indication.

All committee members voted no except for the ODAC patient representative, who voted yes on the proposed new indication because he said he and the patients in the support group he runs very much want to see oncologists have another tool in their armamentarium to treat high-risk CRPC, since there are so few options.

ODAC Meeting This Month Will Review Marqibo for ALL

The next ODAC meeting is scheduled for March 21, to discuss Marqibo (vincristine sulfate liposomes injection—New Drug Application 202497, submitted by Talon Therapeutics). The proposed indication is for the treatment of adult patients with Philadelphia chromosome-negative acute lymphoblastic leukemia in second or greater relapse or whose disease has progressed following two or more treatment lines of anti-leukemia therapy.