Denise Myshko

Oncology KOLS: AN IMPORTANT PIECE OF THE PUZZLE

Key thought leaders are influential in the oncology space, and engaging them in clinical trial design and postmarketing programs is critical for success.

The oncology market is changing. Scientific advances are transforming cancer treatments, with outcomes for patients improving. At the same time, patients are challenged by access concerns and high costs of cancer therapies. Earlier diagnosis, longer treatment durations, and increased effectiveness of drug therapies are contributing to rising levels of spending on medicines for cancer care.

The need to address these concerns and provide more complex scientific information means that medical affairs and medical science personnel are becoming more important, experts say.

In a survey of 156 community oncologists who participated in a recent Cardinal Health Specialty Solutions summit, the majority (60%) indicated that national key opinion leaders have the most impact on their treatment behavior.

"The field is advancing rapidly with mountains of new clinical data being published every day," says Jennifer Fillman, VP and general manager at Cardinal Health Specialty Solutions. "No one physician can be an expert across all the topics, tumor types, and biomarkers. As a result, community oncologists will rely on experts who specialize in a particular tumor or state to inform them of new and better diagnostics and treatments."

Thought leaders in the field are more than usually influential, and engaging them in clinical trial design and expanded access programs is critical, say industry researchers at IMS Health. Gaining access to physicians requires having the "right" talent and mix of medical and business skills on board. Increasingly, physicians prefer speaking with medical liaisons.

FAST FACT

THE ONCOLOGY DRUG PIPELINE IS FAR LARGER THAN ANY OTHER THERAPY AREA ACROSS THE PHARMACEUTICAL INDUSTRY, WITH 6,484 PRODUCTS IN ACTIVE DEVELOPMENT ACROSS ALL INDICATIONS.

Source: GBI Research

Thought leaders are the first adopters of most oncology drugs, says Maria Whitman, managing principal and leader of the oncology and specialty therapeutics practice at ZS.

"In oncology, even more so than other specialty areas, thought leaders specialize in a category and the volume of patients they see is substantially higher than the average oncologist," she says. "Many times, early adopters have been involved in the clinical trials and have gained experience with a particular therapy. They are the ones who make an early assessment of the drug and, therefore, they are important both for initial uptake of the drug as well as for influencing trials broadly."

Oncology is the largest therapeutic area within specialty medicine, and the market is expected to double by 2018.

Liviu Niculescu, M.D., VP of global medical affairs at Takeda Oncology, says many opinion leaders have led trials that changed the standard of care, and they do this mostly through networks of researchers.

"These types of clinical research networks aren't found outside of oncology," he says. "These networks in the United States are often cooperative groups, supported by the National Cancer Institute. The involvement of U.S. government helps to build these networks and makes the research much more effective — and much more driven by thought leaders."

He says in oncology, key opinion leaders are connected with each other and it is a much closer community than found, for example, in the primary-care setting.

"These oncologists run trials together, they sit on the same steering committees for trials, they consult with the FDA on common trials, and they are part of cooperative groups," he says. "As a whole, this is a much smaller group of physicians. Pharma companies have to be very conscious of this connectivity and the cooperatives' groups' research interests."

Takeda has an in-house team of medical science liaisons whose key role is to make connections with these thought leaders.

"Our MSLs would be, for example, looking

Thought leaders in oncology often specialize in a particular cancer. This means companies have to be more specific in the type of information they are sharing on how the drug works, especially now with the shift toward targeted therapies.

KATHLEEN MCCONNELL
Cello Health Communications

We facilitate relationships with KOLs. Once people meet each other, it's a whole different dynamic.

KENNETH WAGGONER
PharmaCyte

to create relationships with the thought leaders in such a way that they understand where their research interests are, if they are currently running a trial, and the next opportunity for a KOL to run a trial," Dr. Niculescu says. "The MSLs' focus is on the key opinion leaders and the top researchers and we don't measure, for example, the frequency of calls as is often done with the salesforce. The work of the MSLs is driven by research interests versus the commercial business."

Thought leaders, Ms. Whitman says, are behavioral guides and can influence other physicians and payers.

"They can truly be core coverage influencers, helping to address access and coverage by insurance companies," she says. "Oncology is a unique category. Compendia listings, which are driven by thought-leading oncologists, are the primary threshold for reimbursement, rather than FDA approval. Payers look to thought leaders because they explicitly incorporate compendia listings into their coverage policies."

Additionally, Ms. Whitman says, oncology thought leaders could be life-cycle innovators.

"Investigator-initiated trials are often done by thought leaders, and they are experimenting with ways to use a particular molecule in combination or in different tumors and indications," she says. "They are the ones who are looking at the molecules and asking if they have the potential to help another population of patients. In oncology, we're seeing that experimentation does lead to different uses for a product whether or not the company can promote some of that information. This creates opportunities for life-cycle extensions."

Thought Leaders in R&D

Involving the thought leaders into the very early phases of research is very important, says Stefano Buono, CEO of Advanced Accelerator Applications.

"It's important to establish a scientific collaboration," he says. "We have to get the interest of the investigator before the process begins, even before Phase I or Phase II."

He says the company has three investigator-initiated clinical studies for Annexin and is discussing others. Annexin is a diagnostic candidate for the assessment of apoptotic and necrotic processes, which are present in a number of pathological conditions in oncology and cardiology, as well as in autoimmune disorders. Annexin is currently in Phase I/II clinical trials.

"It's important to have opinion leaders involved with the research of a new drug and understand the efficacies from their direct experience," Mr. Buono says.

Biotech company PharmaCyte is another company that relies on thought leaders for its clinical development programs.

"KOLs are purely and simply leaders in their field and as such are fully knowledgeable of the latest developments in their areas of expertise," says Gerald Crabtree, Ph.D., chief operating officer of PharmaCyte. "In developing a clinical program, their advice and counsel can be invaluable, particularly in structuring clinical trials. By heeding their counsel, overall clinical development timelines can be shortened and drastic mistakes that might otherwise be made can be avoided, both of which can have beneficial impact upon the costs of conducting clinical trials.

"In addition, in some cases, a KOL can assume the role of principal investigator (PI) for a clinical trial," Dr. Crabtree continues. "The PI is responsible for coordinating how the clinical trial is conducted, a particularly important duty when multiple study sites are involved.

There needs to be a better understanding about how oncology treatments can improve the lives of patients so that the cost discussion is not just a business deal.

ERIK DALTON
Healthcasts

From our point of view, for these and other reasons, the involvement of KOLs can be crucial in ensuring the best chance for success of a clinical drug development program."

R&D efforts at PharmaCyte Biotech are based on the use of a proprietary form of live cell encapsulation known as Cell-in-a-Box; this is a platform upon which treatments for serious and even deadly diseases can be built.

PharmaCyte Biotech's treatment for pancreatic cancer consists of a combination of live cells encapsulated using the Cell-in-a-Box technology together with low doses of the anticancer prodrug ifosfamide. Cancer prodrugs must be converted (activated) into their cancer-killing forms for them to be effective.

There will be increasing reimbursement scrutiny around oncology treatment choices, so research and opinions from thought leaders will help to ensure the right patient receives the right treatment at the right time.

JENNIFER FILLMAN
Cardinal Health Specialty Solutions

The live cells that are encapsulated are capable of carrying out this conversion. The treatment represents a form of "targeted" chemotherapy. The company is also using the platform to research breast cancer, brain cancer, and type 1 diabetes.

Kenneth Waggoner, CEO of PharmaCyte, says the key in working with KOLs is communication.

"A lot of doctors and scientists of international repute work in silos; they're standalone all-stars, and they're not used to working across lines," he says. "We've found that our relationships are driven by getting our team of doctors and scientists to know each on a regular, face-to-face basis. Scientific research should be a cooperative effort. Even though there has been a revolution in communication the past decade or so, there is simply no substitute for face-to-face time among our KOLs in building meaningful relationships."

Thought Leaders in the Postmarketing Environment

ZS has found that pharma and biotech companies' access to oncologists, in terms of approved and marketed products, is among the lowest of all specialties. In fact, about half of all oncologists studied place heavy restrictions on rep access.

But many of these oncologists will engage with pharma reps via digital channels. These channels help extend a pharma and biotech company's reach with this specialty group by 35%.

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STEFANO BUONO
Advanced Accelerator Applications

"Across the board, oncologists themselves are harder to reach," Ms. Whitman says. "With KOLs or thought leaders, the information needs and what they are looking for from a pharmaceutical company are much deeper than what you see in other categories, and it is deeper in several ways. The engagement becomes a much more complex conversation and it is the type of conversation that a traditional field rep may not be able to have."

One of the reasons for the depth of conversation needed is that thought leaders in oncology often specialize in a particular cancer, says Kathleen McConnell, managing director, Scifluent, at Cello Health Communications.

"This means companies have to be more specific in the type of information they are sharing on how the drug works, especially now with the shift toward targeted therapies," she says. "These physicians are going to have to have a greater understanding of the subtleties and intricacies of the disease and how to treat specific subpopulations."

Additionally, Ms. Whitman says the conversations with oncology thought leaders may often go beyond the label.

"These specialists want to talk about all of the possibilities of a drug, the way the pipeline or molecule is being developed, how a treatment correlates to other products," she says.

In this environment, the medical affairs team and the medical science liaison become much more important.

"Thought leaders are looking for the ability to discuss the science in a deeper way,

Beyond establishing value, thought leaders are emerging as stewards of responsible spending. Many thought leaders are now speaking about being value conscious and trying to assess value not just on clinical attributes, but also on therapy costs.

MARIA WHITMAN
ZS

which requires a different set of individuals," Ms. Whitman says. "Medical affairs, medical directors, and different liaisons who can have some of those conversations in a more meaningful way with thought leaders are essential. In particular, they want to engage in peer-to-peer dialogue on the potential of a molecule, including off-label and clinical development."

The Role of the MSL

Experts say medical affairs and MSL teams will play an even bigger role in the future as more complex therapies, immune therapies, gene therapies, and personalized medications become more common.

"One of the key conversations right now is around the integration of targeted therapies and immunotherapies," Ms. Whitman says. "The questions are complex; for example, should the treatment regimen be sequential, should one treatment come before another and for what type of patient, should the treatments be combined, can the toxicity be tolerated?"

These types of conversations necessitate having a depth of scientific knowledge particular to oncology.

"If a company wants to reach oncology thought leaders it needs to have a very knowledgeable field force," she says. "Thought leaders in oncology know the disease better than anyone, and they may even have a better understanding of the drug."

Erik Dalton, executive VP of Healthcasts, says a growing field of interest in oncology is personalized medicine, and pharma and biotech companies have to be prepared with educational materials.

"The key challenges that oncologists face include deciding the best antibody to use on a patient, what test to predict a response, if agents can be safely combined with other therapies for the disease, etc.," he says. "Oncology is a fast-evolving landscape. To solve for educational gaps, physicians look to educational materials with clinical data, thought leaders and other resources to help them distill vast amounts of new information for their busy lives."

Ms. Whitman says when working with thought leaders in oncology, companies need to view these as long-term relationships.

"Companies need to have an end-to-end relationship that is sustainable for any single product," Ms. Whitman says. "This includes clinical studies, starting with investigator-initiated research opportunities through Phase II and Phase III as well as postmarketing studies, including advisory and speaking roles."

Thought Leaders: Feedback and Access

Dr. Niculescu says Takeda engages with thought leaders at the beginning of trial design all the way through to postmarketing trials.

"We constantly ask our advisory boards and steering committees for feedback on how to design meaningful end points for patients as well as meaningful end points for reimbursement for payers inside and outside of the United States," he says. "Our advisors often have insightful ideas around quality of life measurements, healthcare resource utilization measurements, or novel endpoints."

He says it's also important to work with thought leaders to help design postmarketing studies to obtain real-life data that are, for example, representative of the patient population of a certain payer.

"For example, we're working on a registry for ixazomib for treating multiple myeloma," he says. "These data will give us real-life information about this particular patient population and how our drug is being used. We need key opinion leaders to be advocates in registry trials, to help design the trial, interpret the data, and then articulate the value of the findings.

"To create lasting and meaningful research relationships with KOLs in a certain disease you need to demonstrate lasting commitment to patients and to the research field," Dr. Niculescu continues. "At Takeda for example, we have been part of the multiple myeloma community for more than 15 years and we currently have a large and active investigator-initiated study program and a large ongoing company-sponsored program to demonstrate our continued commitment to MM patients."

One of the best ways to engage oncology thought leaders is a live meeting format, although Ms. Fillman says this can be challenging due to the demands on oncologists' time and regulatory requirements. In a recent survey Cardinal Health conducted of 150 oncologists from community and hospital settings, 86% indicated that live advisory board meetings are the preferred way to engage with drug manufacturers.

When live engagement is not possible, social networking and other technology-enabled solutions are proving to be effective ways to interact with thought leaders, Ms. Fillman says.

"These digital channels provide timely and cost-effective means to reach thought leaders, but the content needs to be engaging and deliver value," she says. "We have been successful in teaming scientific experts with online content delivery specialists to ensure that the messages are meaningful and are presented in a way that is appealing."

Ms. Whitman says beyond establishing value, thought leaders are emerging as stewards of responsible spending. Some thought leaders are now speaking about being value conscious and are assessing value not just on clinical outcomes but looking at what the therapy is "worth" in terms of costs.

"Since these physicians are also the ones who are experimenting with molecule combinations — which are likely novel and expensive medications — they see part of their responsibility to evaluate the sustainability of the drugs from an economic perspective," Ms. Whitman says.

According to a report released by the IMS Institute for Healthcare Informatics, global spending on oncology medicines — including therapeutic treatments and supportive care — reached the $100 billion threshold in 2014.

Doctors and payers are starting to object to the prices of oncology drugs. In fact, in July in the Mayo Clinic's medical journal, doctors from Mayo Clinic, the University of Texas MD Anderson Cancer Center, Dana-Farber Cancer Institute, and the University of Chicago write that 10% to 20% of patients don't take their treatments as prescribed and say the out-of-pocket costs are bankrupting many patients.

"There will be increasing reimbursement scrutiny around oncology treatment choices, so research and opinions from thought leaders will help to ensure the right patient receives the right treatment at the right time," Ms. Fillman says.

The Oncology Market

- The global oncology market, including drugs used in supportive care, increased 10.3% in 2014 and reached $100 billion, up from $75 billion five years earlier. The CAGR in spending over the past five years has been 6.5% globally. Targeted therapies now account for almost 50% of total spending and have been growing at 14.6% CAGR since 2009.
- Clinical outcomes are improving for major cancers. In most instances, five-year survival rates have risen through continuous and small improvements in detection and treatment, including refinements with existing treatments and gains from new treatment options. Therapeutic effectiveness in multiple genetic subpopulations is being improved through the use of real-world evidence from deep biomarker data linked to treatment information. Molecular diagnostics are transforming development and patient selection, but only one-third of new oncology drugs have an identified biomarker at time of launch.
- Patient access to cancer drugs varies across all markets. The availability of new oncology medicines varies widely across the major developed countries, with patients in Japan, Spain, and South Korea having access in 2014 to fewer than half of the new cancer drugs launched globally in the prior five years. In pharmerging markets, availability of newer targeted therapies remains low but is increasing.
- Even among wealthy countries, new drugs may not be reimbursed. Average therapy treatment costs per month have increased 39% in the United States over the past 10 years in inflation-adjusted terms. Patient out-of-pocket costs have risen sharply for intravenous cancer drugs, increasing 71% from 2012 to 2013.

Source: IMS Institute for Healthcare Informatics