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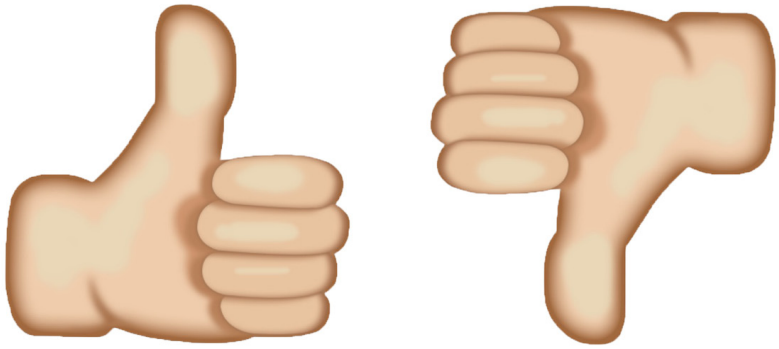

Lilly Drug to Change Squamous NSCLC, But ODAC's Opinion is Nuanced

By Paul Goldberg

The FDA Oncologic Drugs Advisory Committee July 9 appears to have recommended approval for the Eli Lilly and Co. agent necitumumab.

Yes, the word "appears" has indeed appeared in the previous sentence.

It had to because, in breaking with a long-standing tradition, the agency asked ODAC members to "discuss" the key questions of risk vs. benefit of the experimental therapy instead of reducing their answers to a yea or nay vote.

No vote was taken, but The Cancer Letter's analysis of ODAC's discussion suggests that, had a vote been taken, necitumumab would have received an overwhelming 11:1 vote in favor of approval.

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Do-It-Yourself Guide to ODAC Circle One: Yes, No, Maybe

FDA has often asked ODAC members to discuss broad scientific questions. However, the approval questions have, without an exception, been shoehorned into the up-or-down dichotomy.

What is ODAC without a vote on approval questions?

(Continued to page 4)

Huntsman, UNM, and UT Southwestern Receive NCI Comprehensive Designations

Three cancer centers have been awarded comprehensive status from NCI, the highest designation possible: the Huntsman Cancer Institute at the University of Utah, UT Southwestern's Harold C. Simmons Cancer Center, and the University of New Mexico Cancer Center.

A fourth, the Dan L. Duncan Cancer Center at Baylor College of Medicine, is also expected to receive the comprehensive designation, sources said. This will bring the total number of comprehensive centers to 45.

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Has ODAC Become a Game Without a Scoreboard?

(Continued from page 1)

Thus, it's a fair guess that the agent is heading toward becoming a part of front-line treatment of locally advanced or metastatic squamous non-small cell lung cancer.

Approval of this Biologics License Application is important, because the treatment of squamous NSCLC hasn't changed in over 15 years. Necitumumab would be used in combination with a doublet treatment of gemcitabine and cisplatin.

Apparent (that word again; sorry) procedural change at FDA is a landmark as well. If the agency indeed intends to solicit discussion rather than votes from its clinical advisors, it will acquire far more flexibility in making approval decisions.

In the era when cancer care becomes increasingly specialized, this is certain to have an impact on what actually gets approved.

In the past, the agency has asked its advisors to discuss broader questions, but for as long as anyone can remember, approval questions were put to the vote.

The difference in format is profound:

Asking ODAC members to boil down their opinions to the format of a book-jacket blurb as opposed to an up or down recommendation would in effect allow the agency to hit the replay button and control for lapses of understanding, the absence of expertise—and, of course, posturing.

In the past, the agency's final decisions usually went by the recommendations of its outside advisors.

Alas, in some cases voting committee members clearly failed to grasp the text of regulations. (The standard for granting accelerated approvals—"reasonably likely to predict" clinical benefit—has been demonstrated to confound some of the greatest minds of medicine.) On occasion, vocal members have led the rest of ODAC into proverbial rabbit holes and off proverbial cliffs. And there have been times when resident luddites pushed the wrong button, voting for approval while intending to vote against, and vice versa.

"One of the reasons we do not have a vote—I keep on emphasizing—we are more interested in your underlying reasons in the discussions here rather than a vote," FDA's cancer czar Richard Pazdur said after the ODAC discussion concluded. "The agency will make a determination on this application. If somebody asked me when it will be before the due date—on or before the due date—so stay tuned."

Asked by stunned reporters whether ODAC discussions have permanently displaced votes, Pazdur, director of the agency's Office of Hematology and Oncology Products, didn't provide a definitive answer.

The absence of a vote can be bewildering. Is ODAC becoming a game without a scoreboard? To find out how the day's discussion would have translated into votes, one will have to sharpen a No. 2 pencil and carefully go through the transcript of the meeting's concluding act.

This story provides the opportunity to do just that. (See below.) ODAC can still be covered, but if this effort is an indication, it would take roughly 4,000 words.

Even without a vote, Lilly officials seemed to be pleased with their appointment with ODAC.

"We are encouraged by the committee's constructive discussion on the benefit-risk profile of necitumumab as few advances have been made over the past two decades in the first-line treatment of advanced squamous NSCLC, leaving a significant unmet medical need," Richard Gaynor, senior vice president for product development and medical affairs for Lilly Oncology, said in a statement. "We believe necitumumab with gemcitabine and cisplatin represents a meaningful advance in the search for a new first-line treatment option and look forward to working closely with the FDA as they continue their review."

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The Question at Hand:

ODAC was asked to address the question that has become something of a classic: Does the increase in overall survival in this case constitute a clinical benefit?

In this case, the addition of necitumumab resulted in a statistically significant 1.6 month median improvement in overall survival and a 0.2 month improvement in median progression-free survival, compared to gemcitabine and cisplatin alone in patients with squamous NSCLC.

The trial was conducted in the first-line setting.

Necitumumab is a second-generation recombinant human monoclonal antibody that binds to the extracellular domain of the human epidermal growth factor receptor and blocks interaction between EGFR and its ligands.

Lilly's application was based on a phase III trial, called SQUIRE, a randomized, controlled, open-label, international study that enrolled 1,093 patients with advanced squamous NSCLC who had not received prior chemotherapy for metastatic disease.

Squamous and non-squamous NSCLC are two different diseases that are treated differently. When the company tested the agent in non-squamous disease in another trial, called INSPIRE, the data monitoring committee noted an imbalance in the number of deaths attributed to potential thromboembolic events and deaths of all causes in the experimental arm, and the trial was stopped.

On the safety side, necitumumab produced adverse events that were generally consistent with those seen with other anti-EGFR agents.

In its questions for ODAC, FDA focused on the incidence of thromboembolic events that were higher in the necitumumab arms in the company's two trials. In the SQUIRE study, which focused on squamous disease, the incidence of grade 3 or greater TEs were 9 vs. 5 percent. TEs were 11 vs. 6 percent in the INSPIRE trial, which focused on non-squamous disease.

Much of discussion at ODAC focused on the 9-percent incidence of hypomagnesemia seen in SQUIRE. However, it was unclear what role this adverse event played in causing death. It was also unclear whether pretreatment with anticoagulants would be appropriate.

FDA posed two questions to ODAC:

• Do the efficacy and safety results of SQUIRE in squamous cell NSCLC support a positive benefit/risk assessment of necitumumab in combination with gemcitabine/cisplatin in the proposed population?

• Do the INSPIRE trial results in the non-squamous NSCLC population impact the benefit/risk assessment of necitumumab for squamous NSCLC?

Patients with first-line squamous disease have few treatment options, and this situation hasn't changed in two decades, even as treatment were added for other settings in lung cancer. In first-line squamous disease, guidelines call for a platinum-based doublet of cisplatin or carboplatin combined with gemcitabine, vinorelbine or a taxane.

These patients are not candidates for pemetrexed or bevacizumab. EGFR mutations and ALK translocations are very rare among patients with squamous NSCLC, which is why testing for these genetic aberrations is not recommended for patients with squamous NSCLC, and it is not done routinely.

"When I see patients in my clinic that have squamous cell lung cancer, they and their families have often reviewed the literature, and they know about new therapies in lung cancer," said David Gandara, director of the Thoracic Oncology Program at UC Davis Comprehensive Cancer Center, who spoke on behalf of Lilly. "They ask me, what about bevacizumab? I say unfortunately, not for you. Afatinib? Sorry, not for you. Crizotinib? Sorry, that's for adenocarcinoma.

"Now we actually have a regimen with necitumumab specifically designed for squamous cell patients. We should not underestimate the value of this finding."

Two drugs were recently approved for the squamous NSCLC indication, but not in the front-line and not in combination with chemotherapy.

The new second-line drugs are:

• Ramucirumab, approved in December 2014 in combination with docetaxel, for treatment of metastatic NSCLC (both squamous and non-squamous) with disease progression on or after platinum-based chemotherapy, and

• Nivolumab, approved in March 2015 for patients with squamous NSCLC with progression on or after platinum-based chemotherapy.

"It is important to remember though that only 50 percent of patients ever make it to second line treatment, so we still need better first-line therapies to offer them," said Everett Vokes, physician-in-chief at the University of Chicago Medicine and Biological Sciences, chair of the Department of Medicine, and the John E. Ultmann Professor of Medicine and Radiation Oncology, who also spoke as part of the Lilly presentation.

"Platinum-based doublets have a well-established safety profile and the addition of necitumumab does not exacerbate their known toxicities, in particular febrile neutropenia was not increased.

"Second-line treatment options to existing lung cancer, including squamous cell lung cancer, and have traditionally consisted of docetaxel and recently the addition of ramucirumab.

"In my opinion it would be a favorable benefit risk as a new treatment option. The trial showed clinically meaningful improvement in overall survival and as a clinician I would be comfortable discussing the three drug regimen with my patients."

In SQUIRE, the primary efficacy endpoint was overall survival.

Secondary endpoints were progression-free survival and overall response rate.

The median OS was 11.5 months (95% CI 10.4, 12.6) in the N+GC arm compared to 9.9 months (95% CI 8.9, 11.1) in the GC arm [HR=0.84 (95% CI 0.74; 0.96); logrank p=0.012)].

The median PFS was 5.7 months (95% CI 5.6, 6.0) in the N+GC arm compared to 5.5 months (95% CI 4.8; 5.6) in the control arm [HR=0.85 (95% CI 0.74, 0.98); logrank p=0.02)]. Overall response rate was 31 vs. 29 percent (p=0.40) in the N+GC and GC arms, respectively.

Data from INSPIRE were submitted to provide safety information.

In INSPIRE, patients were randomized 1:1 to receive either necitumumab with pemetrexed and cisplatin or pemetrexed and cisplatin alone. The study was closed prematurely at the request of the data monitoring committee due to an imbalance on the number of deaths attributed to potential thromboembolic events and deaths of all causes observed in the N+PC arm compared to the PC arm.

At the time of the study closure, 633 patients out of 947 planned were enrolled. There was no difference in OS based on the available data [median OS 11.3 vs.11.5 months in the treatment and control arms, respectively (HR=1.01, 95% CI 0.84; 1.21)].

Conor Hale contributed to this story.

Do-it-Yourself Guide to ODAC Circle One: Yes, No, Maybe

(Continued from page 1)

Here, The Cancer Letter has combined a transcript of the ODAC discussion with a coding scale that may provide a clue about how the vote on necitumumab would have gone.

Grzegorz Nowakowski, *assistant professor of medicine, Mayo Clinic Rochester:*

I think this is a well-conducted study, which provides a small but significant benefit in terms of overall survival, which is the endpoint, which captures both safety and efficacy of this combination. The toxicity is acceptable, considering the severity of the disease.

I think there are concerns about the supportive care, which we alluded to, about replacement of magnesium, and thromboembolism prophylaxis, but overall I believe that the risk-benefit ratio appears to be pointing towards the benefit of this combination.

Code this answer (circle one): Yes No Maybe

Michael Menefee, *assistant professor, Division of Hematology and Oncology, Mayo Clinic, Jacksonville, Fla.:*

I would agree that the simple answer to the question is yes, there is a positive benefit risk ratio for this compound, but there are still caveats out there regarding concerns regarding toxicity, and also, to some degree, the magnitude of the overall benefits.

I still think the additional studies that are evaluating this compound in this patient population may bear significant impact on whether or not the results of the study are validated.

Circle one: Yes No Maybe

Bernard Cole, *professor, Department of Mathematics and Statistics, University of Vermont*:

I agree. I think that, yes, there is a positive risk-benefit ratio. Overall survival is really the gold standard, and this trial has demonstrated—I would call it actually substantial, given the disease setting and history of the treatment in this disease setting in relation to other approvals that have been made—that the relative benefit of a decrease in the risk of death by 16 percent, I think, is sizable and substantial. I am very

pleased to see it, actually.

I also think the progression-free survival benefit is important to note. I was less concerned than some around the table about ascertainment bias, and I think the steps that we saw on the curve were really attributable to the fact that those assessments are done at regular time intervals, because progression is an opinion as well.

There's certainly the potential for some bias in that, however I think there is pretty objective criteria for defining progression. So I actually accept that the progression-free survival benefit is also substantial with the 15 percent reduction.

I would have liked to see a little bit more of an evaluation, because we are considering risk-versus-benefit in terms of the time that was actually spent with these serious adverse events is that amount of time is going to weigh into the decision between physicians and patients about whether to actually start treatment, but that's potentially something that the sponsor could do after the fact to help with the decision-making.

Circle one: Yes No Maybe

Deborah Armstrong, *ODAC chair and professor of oncology, the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University:*

I also agree. I think the this is a population for which we really don't have—it's sort of been left behind in the non-small cell lung cancer group, and this may be a very temporary move forward, but we can feel the void for squamous cell patients even if immunotherapy moves up to frontline, there's a significant number of patients who aren't candidates for immunotherapy, because of other disorders.

I certainly think the survival benefit is modest but it's real; it's incremental as Dr. Gandara said, but when I talk to the patients who are going on trials, they all want a magic bullet or a home run, but frankly we tend to build in small baby steps and move forward that way, and this would have to be considered one of those.

I do think continuing ongoing efforts to look at managing the toxicities, which could then even balance further the risk-benefit would be something I would strongly encourage, particularly with regard to the clotting issues in the magnesium issues as we've discussed at length.

I would also encourage being pretty frank about the populations that may or may not benefit and that might include people about no EGFR expression; that don't benefit in the patients 70 or older, and, again, if you take some of those patients out who don't benefit, you might ultimately enrich the population for a little bit greater benefit overall.

Circle one: Yes No Maybe

Bruce Roth, *professor of medicine, Division of Oncology, Washington University School of Medicine:*

I just want to say, echoing what Dr. Pazdur said before, about not making a decision about the drug based upon what might be done down the road—I think we have to make the risk-benefit assessment on what we have here, not based on punitive risk management strategies that may make us feel good, but may or may not save the lives of any patients down the road.

I can certainly hypothesize that for every VTE that we successfully prophylaxically anticoagulate, we have another bleeding death, and so I don't want to make ourselves feel good about risk-benefit down the road, with "well, we could take care of that," when we may not even be addressing the right issues, much less, as Dr. Liebmann said, successfully treating the ones that we've identified.

So I think we need to make the risk-benefit judgment with what we have available here today, not about what might happen in post marketing discussions.

Circle one: Yes No Maybe

Tito Fojo, *senior investigator and director of the NCI Medical Oncology Fellowship Program, Medical Oncology Branch Center for Cancer Research:*

I agree with everything Dr. Roth said, and at the end of the day this trial doesn't provide me the comfort of saying that the risk-benefit is a favorable one. It sure would be nice to have better data and additional data.

So in the end I'm unconvinced—it doesn't mean that there might not be some—but I also recognize this is a difficult disease and everybody's trying to do the best possible. So I'm aware of that. I just wish the data were much better than it is.

Circle one: Yes No Maybe

Louis Diehl, *professor of Medicine at Duke University Medical Center*:

When I sit in this room I think of trials of a thousand people. When I sit in the clinic, I think of trials of one.

This trial of one thousand people informs me of my trial of one in the clinic. What it teaches me is that

I'm going to have to have a discussion with the patient about survival increases, but I'm also going to have a discussion about survival about sudden death, about rashes and about clots—and I would like to have that discussion with the patient.

Circle one: Yes No Maybe

Virginia Mason, *president and executive director of the Inflammatory Breast Cancer Research Foundation:*

Thanks for saying that, because I think that's been an issue in some other things we discussed on this panel, that if physicians will have that discussion, and a really frank discussion, so that patients know what the risk-benefit is, and when you look at this particular study, it was a pretty small group of population that was in the U.S., and I wonder what bearing that may have on who responds and who doesn't respond in terms of also those side effects.

While there is just, in some respects, a very modest benefit, it is a population that needs options. And if I could be assured that people are going to have good monitoring and good discussions about the risk-benefits per patients, I can feel comfortable with this moving forward.

Circle one: Yes No Maybe

Terry Gillespie, ***p****atient representative, Westmont, Ill.:*

I agree with Ms. Mason. Squamous cell lung cancer does not have a lot of options; options we need. However it is kind of scary that the doctors don't also sit down with you and explain the risks—but if that's done then I think this is a wonderful medicine.

Circle one: Yes No Maybe

Brent Logan*, professor and director, Division of Biostatistics Medical College of Wisconsin, Milwaukee:*

Approval from a single trial needs to be based on robust and compelling evidence of clinical benefit in a favorable benefit-risk profile. And I think survival is a compelling endpoint.

It incorporates both efficacy and toxicity.

As we have discussed, we have seen a number of these toxicity concerns raised and as was discussed, I agree that we should look at the data in its current form, and not consider how can we mitigate the risk, because that may or may not work, but overall survival allows us to do that.

It allows us to weigh the benefit and the risk very clearly. And I think patients may be willing to risk some of these toxicities for a survival benefit, so what do we see? We see modest clinical benefit in terms of the magnitude of improvement.

We see consistent results on progression-free survival with similar hazard ratio with progression-free survival to what we had with survival, despite some of the earlier discussion. And the sensitivity analysis is fairly robust, and the subgroup analyses are fairly consistent except for this issue with the inconsistency with age. So I think overall it is fairly robust, and so I feel comfortable.

Circle one: Yes No Maybe

Raffit Hassan*, senior investigator and co-chief, NCI Thoracic and GI Oncology Branch Center for Cancer Research:*

I think that the overall survival is modest, but I think it is significant and meaningful, especially considering the patient population with performance status 2, increased tumor burden, so I think it does present an improvement in the treatment of squamous cell lung cancer patients.

And in terms of the toxicity, we discussed about so, I think hypomagnesemia, as well as the DVT issues could be managed with better education and both of the providers having a discussion with the patients.

Overall, I think it does represent a benefit to the patient.

Circle one: Yes No Maybe

James Liebmann*, assistant professor of medicine at the Department of Medicine, University of Massachusetts:*

I think I said at the outset of this discussion that I thought that the data showed a positive benefit-risk in that there's modest, real survival benefit.

And the additional risk is what you almost would've expected from something that affects EGFR, and so I think in that regard I agree with what most folks have said here.

I will say, philosophically, I think it's interesting to have how drugs or how anything in life pops up.

It's been six years since the FLEX study was published which used cituximab in a similar patient population with platinum that showed an almost

identical survival benefit, and the only reason I get that we don't talk about cituximab is because they picked the wrong chemotherapy drugs and had several neutropenia.

And so I think it's curious that here we are with wholly different chemotherapy drugs but these are the results, so yes I think it's an overall positive.

Circle one: Yes No Maybe

Howard Fingert, *industry representative, senior medical director of clinical research for Millennium, the Takeda Oncology Company:*

As you all know I'm a nonvoting member, but I guess I can be a discussion member.

So several topics raised: I do agree that understanding the value of the drug and utility in the U.S. population is important, but I'm also very impressed by—there's certainly, from an industry perspective, a need for us to appreciate how to evaluate trials like this, that we are going to see over and over again, that are largely done outside the U.S., because there's multiple dynamics going on.

Many in the industry want to do more in the U.S., but some of us, like I was trained in the cooperative groups, you don't want to compete with the cooperative group trials.

So we sometimes are forced to go ex-U.S. to complete these trials and this ODAC group, I think, has reviewed drugs for kidney cancer that were all ex-U.S., and a recently lung cancer drug was approved which was had zero patients in the U.S., maybe one in North America.

In the latter case, we talked about how markers can supersede region, and here we do have a marker this EGFR marker that was so positive, and I do believe that this likely applies here.

Even though it's a small proportion—less than 10 percent, I think—that were from the U.S, I think that the sponsors if anything, should be commended. That's a normative thing, and I wish there were more but we have what we have.

Regarding the subject about my colleagues saw, and they see what they see now, and we cannot just have wishful thinking about what might happen with risk mitigation—from my perspective, I'm seeing something more than just the data here.

I'm also seeing a commitment by the sponsor towards ongoing science, and dynamic engagement about this topic of risk management. They're not just marketers.

The last slide that was shown about the T-MED and different EGFR analysis—I mean I think that kind of exemplifies the fact that the sponsor has a long-standing commitment.

In other words, risk management is not a single point in time, it's in a dynamic commitment, a dynamic process; that will, as new data arises, you have to have people to add a commitment to act on it for the benefit of patient care.

I think that the Alimta example is a telling one.

Many of you remember the early Alimta clinical experience was also bothered by deaths, and it was the sponsor that had the courage to really critically analyze this whole issue of supplementing and educating their trialists and the prescribing community that they must do this through prescriber education and it really mitigated and made the product available throughout the United States and the world now as a major product helping patients with lung cancer.

And it really overcame that death experience that happened with those early versions of that drug.

So that's the way I see it here and thank you for asking my opinion.

Don't code this answer. Fingert is a non-voting member.

Three Centers Get NCI-CCC Designation; Fourth Expected

(Continued from page 1)

Huntsman is the only cancer center to be designated by NCI in the five-state Intermountain West region, including Utah, Wyoming, Montana, Idaho and Nevada, which covers more than 17 percent of the continental U.S. landmass.

The award was the result of an extensive review process that culminated in a full-day on-site visit by national cancer research experts in the fourth quarter of 2014.

"The positive review of HCI's programs by leaders in cancer research recognizes and reaffirms the innovation and impact of our efforts to save lives," said Mary Beckerle, Huntsman's director and CEO. "This NCI designation brings financial resources to support further development of our research infrastructure, keeping us on the leading edge of technology and expertise."

The comprehensive designation recognizes not only the quality of cancer research, training and public outreach programs at HCI, but acknowledges the depth and breadth of research in three major cancer research

areas: laboratory, clinical and population-based research. The designation also recognized HCI for the impact of its research findings on national cancer care guidelines and improved patient outcomes.

"This designation is the result of professionalism and exceptional expertise of our physicians, scientists, and administrative staff at Huntsman Cancer Institute," said Jon Huntsman Sr., HCI's founder and chief benefactor. "Only a small percentage of the nation's cancer programs have the excellence necessary to receive comprehensive cancer center status."

Sen. Orrin Hatch of Utah praised the high quality of cancer research conducted at HCI. "I have nothing but praise for the high quality of the Huntsman Cancer Institute's cancer research, public outreach, and patient treatment," he said. "We are lucky to have such an extraordinary resource in our state. HCI is truly on the cutting edge of cancer research and provides unmatched care for patients during one of the most difficult times in their lives."

HCI's research strategy is to translate genetic understanding of cancer into individualized risk assessment, diagnosis, and treatment. According to HCI, its researchers have earned recognition for their work in identifying gene mutations for hereditary colon cancer, breast and ovarian cancer, melanoma, neurofibromatosis and paraganglioma.

Since its previous evaluation in 2009, when HCI applied and obtained renewal of its cancer center status, it has recruited 33 new program members and garnered 20 percent more NCI funding of its studies. HCI opened more than 60 new collaborative grants and doubled enrollment in clinical trials of cancer treatments in the five-year project period. In addition, building expansion completed in 2011 doubled the size of the cancer hospital, and construction is underway that will double the size of HCI's research facilities upon its completion in 2017.

An NCI-designated comprehensive cancer center must demonstrate depth and breadth of cancer research, as well as substantial transdisciplinary research that bridges these scientific areas and changes cancer care. In addition, a comprehensive cancer center must demonstrate professional and public education and outreach capabilities, including the distribution of clinical and public health advances in the communities it serves. NCI evaluates each of its designated cancer centers every five years.

Simmons Cancer Center is the second facility in the University of Texas System to receive the comprehensive designation, joining MD Anderson Cancer Center in Houston. The designation includes an $8.1 million grant for cancer center support. Simmons was designated an NCI cancer center in 2010.

"The differentiating benefit of comprehensive cancer centers is that they combine quality care with research and technology that advance the treatment and prevention of cancer," said James Willson, professor and director of the Simmons Cancer Center, and associate dean of oncology programs at UT Southwestern.

"The NCI designation underscores our dedication to not only improving results in how we manage disease, but also to making an impact on the community in terms of early detection and management of cancer at its most curable stages."

Partnerships with Parkland Health & Hospital System, Children's Medical Center Dallas, the UT School of Public Health Dallas Regional Campus, and UT Southwestern's Moncrief Cancer Institute in Fort Worth played an important role in achieving the comprehensive designation, said Willson, holder of The Lisa K. Simmons Distinguished Chair in Comprehensive Oncology.

"Partnerships that we have established with affiliated health care providers are an exciting aspect of our cancer center. Parkland is part of our commitment to bring cutting-edge advances in care and prevention to the most vulnerable and underserved in our population," he said. "Children's Medical Center Dallas is crucial to our commitment to pediatric patients. We are all integrated as part of our comprehensive cancer center."

"Integration is what a comprehensive cancer center achieves," said Willson, who has led the center since 2004. UT Southwestern's Simmons Cancer Center includes more than 200 members from over 30 departments and centers campus-wide.

Along with the most recent NCI recognition, the Simmons Cancer Center also is among only 30 U.S. cancer research centers to be named a National Clinical Trials Network Lead Academic Site.

UT Southwestern currently receives more than $100 million annually for cancer research from the NCI and other NIH and peer-reviewed funding agencies, including the Cancer Prevention and Research Institute of Texas.

"The physicians and staff at UNM Cancer Center believe that all New Mexicans deserve access to world-class cancer care in their home state, where they can be surrounded and supported by their family and friends," said Cheryl Willman, director and CEO of the UNM Cancer Center.

"To really serve the people of New Mexico, we have to be one of the nation's very best. And that means being a National Cancer Institute designated cancer center."

The New Mexico state legislature established the cancer center at the UNM Health Sciences Center in 1971, when the state had no doctors specializing in cancer.

The center now has more than 125 oncology physicians and more than 130 cancer scientists. It first achieved NCI designation in 2005 and renewed that designation in 2010. This year they received a merit descriptor of "Outstanding."

The UNM Cancer Center is also founding member of the New Mexico Cancer Care Alliance, which brings access to clinical trials to all New Mexicans. And, it recently joined ORIEN, the Oncology Research Information Exchange Network, to bring a new level of cancer care to New Mexicans by sharing de-identified medical data.

"We could not be more proud of our cancer center and its achievements, which are critical for the growth and vitality of our institution and the citizens of New Mexico," said Paul Roth, chancellor of the UNM Health Sciences Center and dean of the UNM School of Medicine.

UNM Cancer Center uses a cross-linked network of scientists working within four research groups which share research tools and techniques. Scientists also work with other research entities and communities across New Mexico to reach rural and underserved groups.

"We are expected to translate our science from the laboratory or the population or the community all the way to a human being [through clinical trials]," Willman said. "That's the research standard we're held to. That is a huge challenge."

House Passes 21st Century Cures Act

By Matthew Ong and Nick Crispino

The U.S. House of Representatives July 10 passed H.R. 6, The 21st Century Cures Act without amendments by a 344 to 77 vote.

The bill—designed to modernize clinical trials and streamline the drug approval process—would boost NIH funding by $1.75 billion in mandatory funding a year over the next five years, for a total of $8.75 billion, and FDA's budget by a total of $550 million.

The bill was put together by House Energy and Commerce Committee Chairman Fred Upton (R-Mich.), Oversight and Investigations Subcommittee Ranking Member Diana DeGette (D-Colo.), Health Subcommittee Chairman Joe Pitts (R-Penn.), full committee Ranking Member Frank Pallone, Jr., (D-N.J.), and Health Subcommittee Ranking Member Gene Green (D-Texas).

"Today, we took a big leap on the path to cures, but we still have much work left to do. The 344 votes today should be a springboard for action," the bill's sponsors said in a statement. "On to the Senate."

The bill advances initiatives in big data and precision medicine, said American Society of Clinical Oncology President Julie Vose.

"Big data and precision medicine have enormous potential to improve the way we treat cancer. ASCO currently has two major initiatives underway in this arena with CancerLinQ, a big data project aimed to rapidly improve the overall quality of cancer care, and the Targeted Agent and Profiling Utilization Registry Study, our first-ever clinical trial, designed to learn from the real world practice of precision medicine," Vose said in a statement. "Provisions in the legislation will support and aid efforts like these and build an infrastructure that fosters rapid development and dissemination of important advances.

"The 21st Century Cures Act also takes steps to give the FDA the resources it needs to fully carry out its mission and it helps to reverse years of stagnant funding that has eroded the research funding capability of the NIH. The inclusion of more than $9 billion in mandatory additional funding for NIH and the FDA will strengthen both agencies and the medical community as a whole."

The legislation's infusion of funding for NIH and NCI is long overdue, said American Cancer Society Cancer Action Network President Chris Hansen.

"It reflects the broad bipartisan consensus that making research a national priority will lead to advances in the detection and treatment of chronic diseases such as cancer," Hansen said in a statement. "We call on the Senate to take up this important legislation and make much-needed funding for cancer research a reality."

The bill is a victory for patients and their families, said Research!America President and CEO Mary Woolley.

"Medical advances deliver profoundly important returns; preventing illness, restoring health, and saving lives from one generation to the next," Woolley said in

a statement. "The economic returns are also substantial with the development of new therapies and medical devices to maintain our nation's competitive edge in science and technology. Increased funding for the National Institutes of Health and the Food and Drug Administration will support the important work of these agencies in finding and advancing solutions to diseases that continually try to outsmart us.

"We urge the Senate to embrace this opportunity to transform medical innovation, and bring about the kind of progress that helps our nation and its people thrive."

The Drawbacks

Other proposed changes in the 21st Century Cures Act to the health care system could lead to "less salutary" outcomes for patients, according to Jerry Avorn and Aaron Kesselheim, who critiqued the bill in the New England Journal of Medicine.

Avorn is a professor of medicine at Harvard Medical School and chief of the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital. Kesselheim is an assistant professor of medicine at Harvard Medical School and site director of the Fellowship in General Medicine and Primary Care, Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham.

"As introduced, the 21st Century Cures Act instructs the FDA to consider nontraditional study designs and methods of data analysis to further speed approvals," the authors wrote. "Adaptive trial designs and the use of Bayesian methods hold promise in some kinds of evaluations, particularly in oncology.

"However, more problematic proposals include encouraging the use of 'shorter or smaller clinical trials' for devices and the request that the FDA develop criteria for relying on 'evidence from clinical experience,' including 'observational studies, registries, and therapeutic use' instead of randomized, controlled trials for approving new uses for existing drugs.

"Although such data can provide important information about drug utilization and safety once a medication is in use, there is considerable evidence that these approaches are not as rigorous or valid as randomized trials in assessing efficacy."

The bill goes further in altering the requirements for approving medical devices—an area long criticized for lack of rigor as compared with drug evaluations, according to Avorn and Kesselheim.

"As proposed, the new law would redefine the evidence on which high-risk devices can be approved to include case studies, registries, and articles in the medical literature, rather than more rigorous clinical trials," Avorn and Kesselheim wrote.

"Another section would allow device makers to pay a third-party organization to determine whether the manufacturer can be relied on to assess the safety and effectiveness of changes it makes to its devices, in place of submitting an application to the FDA.

"Thus certified by the external company, a device maker would be authorized to continue to assess its own products on an ongoing basis.

"Political forces have introduced other provisions that could lead to the approval of drugs and devices that are less safe or effective than existing criteria would permit.

"Patients and physicians would not benefit from legislation that instead of catapulting us into the future, could actually bring back some of the problems we thought we had left behind in the 20th century."

ORIEN Partners with Three Cancer Research Centers

The Oncology Research Information Exchange Network July 9 announced the addition of three cancer institutions to its precision cancer research partnership, bring the total number of partners to nine.

The new members are the Rutgers Cancer Institute of New Jersey, the University of Southern California Norris Comprehensive Cancer Center, and Morehouse School of Medicine.

"Becoming part of ORIEN adds great opportunities for Rutgers Cancer Institute of New Jersey, enabling discovery based on large-scale, diverse population data as well as patient-specific clinical decision support across a broad, national clinical trial portfolio," said Robert DiPaola, director of the Rutgers Cancer Institute.

Launched In May 2014, ORIEN is a big data research partnership between U.S. cancer centers led by Moffitt Cancer Center and The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

ORIEN is designed to enhance precision cancer medicine efforts already in place at member organizations by enabling unprecedented research opportunities driving greater collaboration. All ORIEN members use a single protocol, Total Cancer Care (The Cancer Letter, March 13).

"It was a natural fit for USC Norris Comprehensive Cancer Center to join ORIEN, as personalized patient care has been a key component of our strategic plan," said Stephen Gruber, Norris' director. "We are proud to partner with ORIEN founders and members to collaborate to change the treatment model for oncology."

To date, more than 124,000 patients have agreed to donate their tissue and clinical data for TCC research to understand cancer at the molecular level. ORIEN members share de-identified data for the development of precision medicine and treatments, which enables researchers and clinicians to match eligible patients to clinical trials and conduct larger and more comprehensive analyses.

"It is increasingly apparent that molecular profiling of tumors will shrink the number of patients eligible for a clinical trial of an agent that targets a specific mutation," said Thomas Sellers, center director and executive vice president of Moffitt. "Bringing on more partners in ORIEN accelerates our ability to conduct such trials. The addition of new centers to ORIEN and their cancer patients to the TCC registry further empowers ORIEN to speed clinical research and provide more than 60,000 cancer patients access to trials that target their specific cancers."

Through federal initiatives aimed at infusing funds into the growing field of precision medicine, ORIEN is growing at a time when the national spotlight is turned to the field's potential and promise to discover targeted treatments.

"We are thrilled to have these leading cancer institutions as part of ORIEN," said William Dalton, CEO of M2Gen. "Together we are building one of the largest and most diverse data warehouse efforts that will allow us to follow and learn from patients to better understand their needs and develop evidence-based approaches to meet those needs."

ORIEN leaders said this recognition illustrates the need for continued collaboration among oncology experts to identify cutting-edge treatments for patients and to improve care.

"ORIEN, in collaboration with leading cancer centers throughout the country, provides cancer patients with greater access to clinical trials specific to their cancer type," said Michael Caligiuri, director of The Ohio State University Comprehensive Cancer Center and CEO of the James Cancer Hospital and Solove Research Institute. "This collaboration and cooperation among a growing number of ORIEN centers means patients may not need to travel far from home to participate.

"The ORIEN network of cancer centers is made up of true partners in data exchange and we are proud to extend these benefits to patients in the form of genomic data research that will help us better understand cancer at the molecular level and hopefully develop more targeted cancer treatments."

James Lillard, associate dean for research at Morehouse, and a professor of microbiology, biochemistry and immunology, said, "The cancer care and research community at MSM has seen significant growth over the past five years; doubling the number of oncologists and quadrupling the amount of translational research funding. Partnering with ORIEN has tremendous potential to propel cancer research forward and reduce cancer health disparities."

Other ORIEN members include City of Hope, University of Virginia Cancer Center, University of Colorado Cancer Center and University of New Mexico Cancer Center. ORIEN operations, through M2Gen, support collaborative research by managing funding, access to data, trial matching governance and client relationships.

In Brief

Britten Named Director of MUSC Hematology/Oncology

CAROLYN BRITTEN was named director of the Hematology/Oncology Division at the **Medical University of South Carolina**. She will continue her role as associate director for clinical investigations at the MUSC Hollings Cancer Center.

Britten was recruited to MUSC in 2012 from the Jonsson Comprehensive Cancer Center at the University of California, Los Angeles, where she held several leadership positions from 2001 to 2012, including associate director of the Signal Transduction and Therapeutics Research Program.

She also holds the Charles Westfield Coker Endowed Chair in GI Oncology at MUSC, part of the South Carolina SmartState Centers of Excellence. Britten has a portfolio of more than 20 actively accruing trials for patients with advanced cancer.

Originally from Canada, Britten received her medical degree from the University of Toronto, and completed internship, residency and chief residency at the University of Western Ontario. She subsequently trained in medical oncology at the University of British Columbia in Vancouver, and completed a research fellowship in cancer drug development at the Institute

for Drug Development at the University of Texas at San Antonio. She then joined the faculty at UCLA, where she developed their solid tumor phase I clinical trials program.

In addition to her phase I clinical trials expertise, she specializes in the treatment of gastrointestinal cancers. Britten has served on multiple committees for the American Society of Clinical Oncology and is highly active in national oncology networks. She recently co-led Hollings Cancer Center's effort to become one of 12 sites funded as a minority-based institutional site for the NCI Community Oncology Research Program which conducts multi-site, NCI-sponsored cancer clinical trials and cancer care delivery research studies.

The Council of the **National Academy of Sciences** approved the nomination of **MARCIA MCNUTT**, editor-in-chief of the Science family of journals, for election as president of the academy, to succeed **Ralph Cicerone** when his second term as NAS president ends on July 1, 2016.

McNutt was elected to the National Academy of Sciences in 2005, and has served on more than 30 committees and boards of the National Academies of Sciences, Engineering, and Medicine. Most recently, she chaired an expert panel that evaluated options for slowing or offsetting global climate change. She is currently a member of the advisory committee for the Division on Earth and Life Studies and the Forum on Open Science.

Her research concentration is in marine geophysics, where she has used a variety of remote sensing techniques from ships and space to probe the dynamics of the mantle and overlying plates far from plate boundaries on geologic time scales.

She is the author or co-author of more than 100 peer reviewed articles and has made important contributions to the understanding of the rheology and strength of the lithosphere. She has demonstrated that a deep-seated, large-scale mantle thermal anomaly has been very persistent. It is not only producing midplate volcanoes in the island chains above its location deep beneath the central Pacific, but also produced older volcanic chains now submerged in the northwest Pacific that erupted as the Pacific plate drifted over the central Pacific over the last 100 million years.

McNutt began her faculty career at the Massachusetts Institute of Technology, where she became the Griswold Professor of Geophysics and served as director of the Joint Program in Oceanography & Applied Ocean Science & Engineering sponsored by MIT and the Woods Hole Oceanographic Institution.

From 2009 to 2013 she was the director of the U.S. Geological Survey, one of the federal government's major science agencies, where she helped lead the response to the Deepwater Horizon oil spill, for which she was awarded the Meritorious Service Medal by the U.S. Coast Guard.

McNutt became the 19th editor-in-chief of Science in 2013. As editor-in-chief she led the effort to establish Science Advances, an open access, online-only offspring of Science.

McNutt is a fellow of AGU, the Geological Society of America, the American Association for the Advancement of Science, the Geological Society of America, and the International Association of Geodesy. She served as president of AGU from 2000 to 2002. Her honors include election to the American Philosophical Society and the American Academy of Arts and Sciences.

A nominating committee chaired by Barbara Schaal, dean of the faculty of Arts & Sciences and the Mary-Dell Chilton Distinguished Professor in the department of biology at Washington University in St. Louis, selected McNutt after a six-month search.

Under the academy's bylaws, the nominating committee puts forward candidates for the presidency for the council's discussion and approval. Although the NAS bylaws permit additional nominations from the membership, this mechanism has never been used.

In the absence of another nomination, McNutt's name will be presented to the full membership for formal ratification Dec. 15. That ballot will also contain the names of candidates for the academy's treasurer and for four positions on the council. Balloting is to be completed on January 31.

KEVIN FITZPATRICK was named CEO of **CancerLinQ LLC**, a wholly owned, non-profit subsidiary of the American Society of Clinical Oncology.

Fitzpatrick, currently the executive vice president

and chief innovation officer of the American College of Cardiology, will begin his new role on Aug. 3.

CancerLinQ will use patient care data from millions of electronic health records, and process and analyze the data to provide feedback and personalized insights.

Prior to joining the ACC, Fitzpatrick was vice president of business development for Lippincott Williams & Wilkins, a publisher of professional health information resources, and managing director of The Duke/Hewlett Packard Center for Outcomes Research and director of the Trauma Research Laboratory at Duke University Medical Center. He is also a 1996 recipient of the Smithsonian Institution/Computer World Healthcare Computing Innovation Award.

In his current role, Fitzpatrick jointly leads the ACC's overall financial management and operational and strategic planning. He also serves as the chief senior liaison between the ACC and its major corporate, EHR, HIT and institutional partners.

Fitzpatrick was instrumental in the creation and implementation of the Diabetes Collaborative Registry, the first global, cross-specialty clinical diabetes registry designed to track and improve the quality of diabetes and metabolic care across the primary care and specialty care continuum.

In addition, he has been very involved in the growth and development of ACC's PINNACLE Registry, cardiology's largest outpatient quality improvement registry, capturing data on coronary artery disease, hypertension, heart failure and atrial fibrillation.

Earlier this year, ASCO announced that CancerLinQ will be developed using SAP HANA, a flexible, multi-purpose data management and application platform created by SAP. Fifteen oncology practices from across the U.S. will adopt the first version of CancerLinQ beginning late in 2015.

MEMORIAL SLOAN KETTERING CANCER CENTER launched a new center, **The Fiona and Stanley Druckenmiller Center for Lung Cancer Research**.

Charles Rudin, chief of thoracic oncology, and David Jones, chief of thoracic surgery, will jointly lead the program. The center will develop and evaluate strategies to treat lung cancer through several initiatives, including basic discovery efforts, preclinical models, and clinical trials.

The center was made possible by a commitment of $25 million from MSK board member Stanley Druckenmiller and his wife, Fiona.

The founding gift to establish the DCLCR is one of many generous contributions Stanley and Fiona Druckenmiller have made to a range of organizations and causes throughout the years, including previous contributions to MSK. Druckenmiller, the former chairman and president of Duquesne Capital, has been a member of MSK's Boards of Overseers and Managers since 1997.

THE AMERICAN COLLEGE OF RADIOLOGY launched the **Commission on Patient Experience**, which will be chaired by **James Rawson**, of Augusta, Ga.

According to ACR, the commission will help develop recommendations on how radiology practices can enhance the experiences of patients and their families; provide information regarding how best to measure radiology patient outcomes; work with other ACR commissions to develop tools, metrics and policy that help members meet Merit-based Incentives Payment System and alternative payment model requirements; and will work closely with the RSNA Radiology Cares Campaign.

THE ASSOCIATION OF COMMUNITY CANCER CENTERS launched the **Institute for Clinical Immuno-Oncology**, an initiative focused on facilitating the adoption of immuno-oncology in the community cancer setting.

ICLIO's goal is to educate medical professionals on the best practices for I-O integration in all aspects of care: clinical care, deciphering reimbursement, insurance, social work and supporting patient access to emerging treatment options.

ICLIO educational tools focus on five primary domains: clinical optimization, coverage and reimbursement, management best practices, patient access and advocacy, and training and development. ICLIO is open to all providers through ACCC. It is estimated that more than 60 percent of all cancer patients in the U.S. are treated by someone in the ACCC network, according to the association.

ICLIO will host its first annual national conference in Philadelphia Oct. 2.

An advisory committee overseeing the planning and development of ICLIO is chaired by Lee Schwartzberg, chief of the Division of Hematology Oncology and professor of medicine at the University of Tennessee, and will be comprised of ACCC members and other I-O leaders.