THE CANCER LETTER

PO Box 9905 Washington DC 20016 Telephone 202-362-1809

Vol. 37 No. 46
Dec. 16, 2011

Pfizer's Inlyta Gives FDA a Teaching Moment: Not All PFS Advantages Are Created Equal

By Paul Goldberg

There were no perplexing clinical questions in sight on Dec. 7, when the FDA Oncologic Drugs Advisory Committee considered Pfizer drug Inlyta (axitinib), an oral vascular endothelial growth factor inhibitor for advanced renal cell carcinoma after failure of a first-line systemic therapy.

The committee recommended approval in a 13-0 vote. The drug met the bar. Clinical data were a no-brainer.

Generally, FDA consults ODAC for one of two reasons:

• The classic reason to convene the committee is to seek guidance on the clinical significance of an application. In these cases, the committee often gets to say no.

• A less common reason is to make a point about the standards for drug approval. In these cases, the agency gets to teach.

(Continued to page 2)

Bioinformatics

caBIG Architect Kenneth Buetow Resigns As NCI Cuts, Reshapes Program He Built

By Paul Goldberg

Kenneth Buetow, architect of the NCI bioinformatics program caBIG, announced that he would leave the institute.

The system that Buetow developed was envisioned during a very different time, when NCI Director Andrew von Eschenbach was pledging to end suffering and death due to cancer by the year 2015.

Buetow presided over a massive enterprise, relying on contractors,

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Anil Potti Explains

Potti: "Coming from India, I Did Not Know This Was Not the Real Rhodes Scholarship"

In a letter to the South Carolina Board of Medical Examiners, former Duke University cancer researcher Anil Potti elaborated on his reasons for stating incorrectly that he had been a Rhodes Scholar.

In the document dated Jan. 11, 2011, obtained by The Cancer Letter, Potti stated that he was a nominee for another award, which involved India's Ministry of Defense, and "coming from India," he did not know this wasn't an official Rhodes Scholarship.

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The Cancer Letter
will take a holiday break
Next Issue:
Jan. 6

Inlyta In Line To Become Drug No. Seven For RCC

(Continued from page 1)

Inlyta appears to have been taken to ODAC because FDA wanted a teaching moment to point out that a two-month advantage in progression-free survival could have an astonishing range of meaning, depending on the disease and the structure of the clinical trial.

Pfizer's Inlyta added two months to PFS, which is something it had in common with another drug in another indication: Genentech's Avastin (bevacizumab), in breast cancer. Actually, in recent years, the question of how much PFS is enough has become the most important question in drug approval.

"Not very long ago, we discussed how two months in improvement in progression free survival in the case of Avastin in breast cancer is not a clinically meaningful endpoint," said ODAC Chair Wyndham Wilson, chief of the Lymphoma Therapeutics Section at the NCI Center for Cancer Research.

"It's very important to keep this in the right context," Wilson continued. "And that is why it is impossible to give a number across all different segments. You know regulatory threshold when you see the actual indication.

"I think that two months for Avastin in that setting was a very different situation that two months here, because here we are determining [whether it is] more unsafe than current tyrosine-kinase inhibitors, which we all agree are different, but not more unsafe. We only need to show that it has activity, and it has equivalent—perhaps somewhat better—activity."

Though Inlyta in renal cell carcinoma and Avastin in breast cancer produce similar margins of improvement in PFS, these numbers mean very different things.

Avastin's effect was additive to chemotherapy. Inlyta's is an advantage over an active control, which means the margin of improvement—two months—should be added to the effect of active control, which is four months.

Inlyta was compared to a recently approved therapy in a superiority trial.

This was a gutsy move on Pfizer's part, far more courageous than launching a trial measuring an add-on effect over a less effective drug. (A non-inferiority trial would have been theoretically possible, though it's unclear how non-inferiority trials to measure PFS should be structured.)

The role of active control is particularly important in advanced renal cell carcinoma, an indication where FDA has recently approved six agents that target tumor angiogenesis and tumor cell proliferation. All but one of these new drugs, approved between December 2005 and October 2009, were approved based on registration studies that included a PFS primary endpoint and either placebo or interferon-alpha on the control arm. (The only exception was the kinase inhibitor Torisel [temsirolimus].)

After Inlyta is approved, oncologists would be able to choose between seven therapies for what amounts to a fairly rare cancer. All of these therapies showed improvement in progression-free survival, and choosing between them would be largely a matter of opinion.

This growing cluster of therapies leaves some observers wondering how it would be possible to come up with strategies for sequencing them.

The Cancer Letter asked Robert Motzer, an attending physician in the Genitourinary Oncology Service at Memorial Sloan-Kettering Cancer Center, and co-principal investigator on the Inlyta pivotal trial, to discuss the issues raised by the introduction of six—soon to be seven—drugs for the treatment of this disease. The Q&A appears on page 4.

Sorting Through Therapies Is Not FDA's Function

In addressing the committee, Richard Pazdur, director of the FDA Office of Hematology and Oncology Products, said PFS in advanced renal cell carcinoma is a long-established standard for regular approval in advanced renal cell cancers.

"We have six drugs that have been approved—and

THE CANCER LETTER

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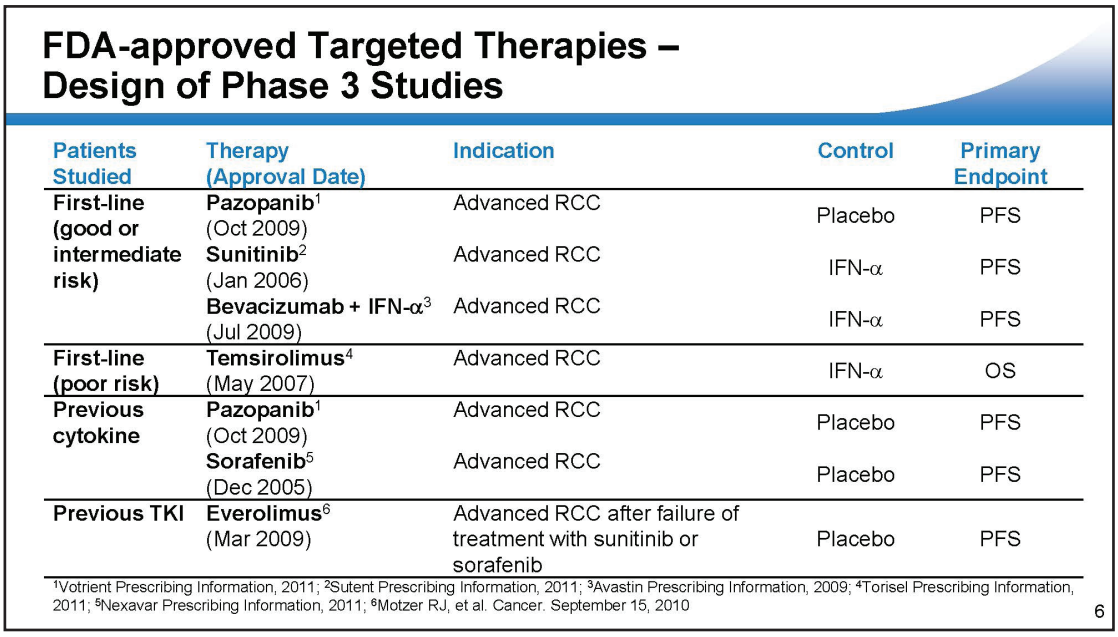
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
General Information: www.cancerletter.com

Subscription $395 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc.

five companies did it with a PFS endpoint—we can't hold one sponsor to a higher standard than another sponsor," Pazdur said.

"We also have data that this drug demonstrates an overall progression-free survival advantage over a recently approved drug."



FDA-approved Targeted Therapies – Design of Phase 3 Studies

Patients Studied	Therapy (Approval Date)	Indication	Control	Primary Endpoint
First-line (good or intermediate risk)	Pazopanib[1] (Oct 2009)	Advanced RCC	Placebo	PFS
	Sunitinib[2] (Jan 2006)	Advanced RCC	IFN-α	PFS
	Bevacizumab + IFN-α[3] (Jul 2009)	Advanced RCC	IFN-α	PFS
First-line (poor risk)	Temsirolimus[4] (May 2007)	Advanced RCC	IFN-α	OS
Previous cytokine	Pazopanib[1] (Oct 2009)	Advanced RCC	Placebo	PFS
	Sorafenib[5] (Dec 2005)	Advanced RCC	Placebo	PFS
Previous TKI	Everolimus[6] (Mar 2009)	Advanced RCC after failure of treatment with sunitinib or sorafenib	Placebo	PFS

[1]Votrient Prescribing Information, 2011; [2]Sutent Prescribing Information, 2011; [3]Avastin Prescribing Information, 2009; [4]Torisel Prescribing Information, 2011; [5]Nexavar Prescribing Information, 2011; [6]Motzer RJ, et al. Cancer. September 15, 2010

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A slide from Pfizer's presentation to ODAC Dec. 7.

Pazdur focused on the approval standards:

"Let me revisit regulatory reality here," Pazdur said. "We are talking about regular approval. Regulatory approval carries with it the obligation that one demonstrates safety and effectiveness. There is no requirement that one demonstrate *superior* safety and efficacy.

"Obviously, if we had a drug that was markedly inferior in its safety profile or an efficacy parameter, then we would have to address this. That is not the case here.

"We do not have a comparative efficacy standard here. It is a demonstration of safety and efficacy. And has the sponsor done that?

"We are dealing with life-threatening diseases in advanced renal cell cancer. In non-life-threatening diseases, multiple, multiple drugs—many of them me-too drugs—are approved on the basis of placebo-controlled trials.

"We are able to use placebo-controlled trials because these other diseases are non-life-threatening. Here, when we are dealing with a life-threatening disease we have to use an active comparator considering the multiple drugs approved in the indication.

"And when you are doing active-controlled trials, particularly against a recently approved drug—the issue from the regulatory perspective is the magnitude of difference between the two arms. If there is a delta of approximately two months in median progression-free survival between the two arms, one needs to add that on to the control effect of the drug that you are comparing it to.

"So that's what we are talking about. What is the effect? It's two months plus the effect size of sorafenib.

"Again, we don't have a comparative efficacy standard. Given that, a company could do a non-inferiority trial to demonstrate efficacy. That would be problematical in this situation, where we have approved the comparator on the basis of one trial.

"If we were talking about an accelerated approval, then you need to be better than an available therapy, since we are approving the drug on the basis of a surrogate endpoint.

"The issue here is what is the control effect of sorafenib? I realize that we do not have a randomized trial of sorafenib in patients previously treated with sunitinib. This is not a perfect world. But what would we feel comfortable with?"

The application was based on a randomized, open-label, multicenter, multinational phase III study that compared axitinib to sorafenib in patients with advanced RCC after one prior systemic first-line regimen containing one or more of the following: sunitinib, bevacizumab and IFN-a, temsirolimus, or cytokines. Altogether, the trial enrolled 723 patients.

In the primary analysis, a statistically-significant and clinically-meaningful improvement in PFS with Inlyta treatment compared with sorafenib treatment was observed. The hazard ratio was 0.665 (95% CI: 0.544, 0.812; stratified log-rank 1-sided $p<0.0001$) indicating a 33 percent reduction in risk of progression or death (median PFS 6.7 vs. 4.7 months).

In the prior sunitinib-containing subgroup (n=389),

the risk of disease progression or death was decreased by 26 percent for Inlyta compared to sorafenib (HR=0.741 [95% CI: 0.573, 0.958] with a p-value of 0.0107 based on 1-sided log-rank test stratified by ECOG performance status).

In the prior cytokine-containing subgroup (n=251), the risk of disease progression or death was decreased by 54 percent for Inlyta compared to sorafenib (HR=0.464 [95% CI: 0.318, 0.676] with a p-value of <0.0001 based on a 1-sided log-rank test stratified by ECOG performance status).

The overall response rate (complete response plus partial response) as assessed by blinded IRC favored Inlyta; ORR was 19.4 percent vs 9.4 percent (1-sided p=0.0001) with a median duration of response of 11 months (95% CI: 7.4, not estimable) and 10.6 months (95% CI: 8.8, 11.5) for Inlyta and sorafenib, respectively.

A planned interim analysis of overall survival was performed to coincide with the primary analysis of PFS, at that time 223 of the required total of 417 death events had accrued. The observed hazard ratio was 1.008 (95% CI: 0.774, 1.313) with a 1-sided p-value of 0.5253 adjusted for ECOG performance status and prior treatment regimen.

At the time of the interim analysis with the median follow-up in each arm of approximately 11 months, 248 patients (68.7 percent) in the Inlyta arm and 252 patients (69.6 percent) in the sorafenib arm were censored.

The final overall survival data are not yet available.

MSKCC's Motzer Discusses Renal Cancer Drugs With TCL

The Cancer Letter asked Robert Motzer, an attending physician at the Genitourinary Oncology Service of Memorial Sloan-Kettering Cancer Center, and co-principal investigator on the Inlyta pivotal trial, to discuss the issues raised by introduction of six—soon to be seven—drugs for the treatment of this disease. The interview was conducted by Paul Goldberg, the editor of The Cancer Letter.

PG: *Why are there so many drugs in renal cancer? It's a fairly rare disease. What's so special about it that would lead to such an explosion of activity?*

RM: It's very interesting. I've been here at Memorial Sloan-Kettering since the 1980s, and my area of focus is kidney cancer treatment and research. One part of this phenomenon is that for many years there has been very little in the way of medications to offer people with advanced kidney cancer. It's been historically one of the most difficult cancers to treat. There simply weren't any chemotherapy drugs that were effective for this cancer.

We studied one chemotherapy drug right after another, without success, and even today it's considered the model for the chemotherapy-resistant cancer. The only medications that seemed to have some effect—albeit very little—were cytokine treatment, and the only drug until 2005 that was approved in the U.S. was interleukin-2 given at high doses. But a very small percent of people—probably about 4 percent—benefited from IL-2, a highly toxic treatment.

Another cytokine, interferon, was a milder treatment. It was used widely in the US and in Europe, although it wasn't approved for that indication in the U.S., and there was controversy in terms of whether it was really beneficial.

So there was a high unmet need for drugs to treat advanced kidney cancer, and for many years the picture was quite bleak.

In the 1990's there was a breakthrough in our understanding of the genes that are responsible for making these kidney cancers grow and produce blood vessels to provide nutrients and oxygen to kidney cancer cells. A gene was identified—called the VHL gene, which is responsible for this process.

And once that happened, it identified targets for medications, called "targeted therapies." At the time when the VHL gene was discovered and identified relevant targets, the industry was developing different targeted drugs—and it was recognized that their targeting profile matched up with kidney cancer.

Since there was very little or nothing out there for the patients, they were all studied right away with kidney cancer. In fact, many of these drugs were first studied in kidney cancer, and after showing benefit, later studied in other types of cancer.

Also, the new targeted therapies were largely studied in patients with advanced kidney cancer and found to be beneficial in parallel. The trials were all going on at or around the same time. Each targeted therapy was compared in a randomized phase III trial to either placebo, because there was no real effective therapy, or interferon, and they all beat placebo and interferon. So in a very short time interval, their benefit was recognized.

In this first round of phase III trials the targeted therapies were all compared to the historical treatments; not yet compared to each other. We were left with multiple drugs showing benefit independent of each other, and now we need to sort out what's the best choice for each patient.

PG: *It's unique, though. Is there another area where a whole bunch of drugs come out the gate at the same time?*

RM: That's right. The situation in which there was such rapid identification of multiple drugs for a cancer without treatment options is unique. It may be unprecedented in cancer drug development.

PG: *It really took guts to run this trial versus an active control, as a superiority trial. This was competing against a recently approved, effective drug. You could actually lose. Why take such a chance?*

RM: When sunitinib, sorafenib, bevacizumab, temsirolimus, everolimus and pazopanib were all being studied, there was no approved targeted therapy to compare to. But what we seeing with the axitinib trial is a second generation of studies in RCC, where now that we do have some standard drugs, we can't really compare the new drug to placebo.

We also can't compare it to interferon. So now the comparison will be made to these already approved targeted drugs.

The axitinib trial is one example. Also, another drug, tivozanib, which is also a relatively pure VEGFR inhibitor, is in a pivotal phase III randomized trial, also being compared to sorafenib.

There is another TK inhibitor that's made by Novartis, called dovitinib, which is targeted to VEGF as well as a pathway proposed to be important in developing resistance to the older targeted drugs, and that's being compared to sorafenib as well in the third-line setting.

PG: *So you had no choice but to take a chance. Is that what you are saying?*

RM: It's clear that with six approved drugs the relevant comparison will be to one of the active compounds. That's what we are seeing with the axitinib versus sorafenib and tivozanib versus sorafenib and dovitinib versus sorafenib phase III trials.

PG: *I thought a safer approach, if you are trying to get a drug on the market, is to go against something like interferon.*

RM: These new targeted agents displaced interferon in clinical practice. This was also a striking observation. Interferon was the mainstay of treatment for advanced kidney cancer for about 20 years.

But, the use of interferon in kidney cancer went away almost overnight when sunitinib and sorafenib were approved in 2005 and 2006. There wouldn't be a role for comparing the new drugs to interferon. It's gone.

PG: *One could still take a more cautious approach and run it against something less active.*

RM: Sorafenib seems to have less activity in first-line therapy compared to sunitinib. So I think, of these different drugs, the data suggests that sorafenib is not the most active drug, and therefore has been the choice of comparator for the newer agents.

The right thing to do now as new drugs come along is for them to compare it to one of these six in their particular niche or area, to show either improved efficacy or an improved safety profile.

It would also be important to compare the already approved drugs to see if we can identify if one is better than the other. An example of this is a 1,100-patient trial conducted by GlaxoSmithKline comparing pazopanib to sunitinib.

I refer to that trial as the heavyweight championship of the world in renal cancer, because sunitinib is Pfizer's TKI, and pazopanib is GSK's TKI. They are both approved for renal cancer, and so it's comparing the two head-to-head. The outcome will define the main drug used in first-line treatment for most patients with advanced RCC.

PG: *As I was sitting there at ODAC, I was wondering, why is this thing here anyway? This thing was a slam-dunk, and certainly the vote reflected that. Why do you think the FDA decided to bring it to the advisory committee? Usually, it's either a problem with the application, or a way to make a point to the industry.*

RM: I don't see any downside in giving it to ODAC for review and comment. If anything, it gives confirmation to FDA.

The trial showed that axitinib was more effective, has a different toxicity profile, with some advantages in side effects that are troublesome to patients. Even from the discussion by Richard Pazdur, where he recapped the ground rules for approval, I think all panel members were on board with this.

PG: *I think, to some extent, it was about Avastin. Your two months of PFS are different from their two months. The agency seemed to be saying that the same PFS advantage in these two settings means two very different things.*

RM: I agree with you. Because I think a difference in PFS in advanced metastatic renal cell cancer in second-line there is a different bar than for Avastin in the metastatic breast cancer setting.

PG: *But it also means different things, because one is an add-on, the other is head-to-head comparison.*

RM: Correct.

PG: *That was what Dr. Pazdur seemed to be really driving at. Now, after this drug is approved, there will be seven drugs out there for a very small indication.*

What's a physician to do?

RM: I think it's important to do, as best as we can, to do studies that compare these different drugs in their settings, to see if one is better than another, or has a better safety profile. That's where pazopanib vs. sunitinib study comes in, since it sets this precedent.

Is there a best sequence?

The choice in drugs and sequencing is made from several factors, including effectiveness and safety profile. Treatment is individualized according to the needs of each patient. Oftentimes in first-line therapy we find that the choice is based heavily on efficacy in renal cell carcinoma, but in second and third-line therapy, the safety profile becomes increasingly important in choosing a drug.

These drugs have similarities among adverse events, but they occur in different proportions, and so for some patients one drug may be a better fit over another.

PG: *But who is going to do those studies, where you try to determine the optimal sequence of use of these drugs? Pharmaceutical companies probably won't. Is it a good thing for government-funded trials to sort out?*

RM: Comparative trials would be good for cooperative groups to take on.

PG: *Is that the only place where it could be done.*

RM: I wouldn't say that. There are some company-sponsored studies that could be done to gain advantage of one already approved drug over another in a particular setting, for marketing purposes. In addition, some regulatory agencies like the FDA or EUA may demand post-approval comparative studies or additional studies.

PG: *Have we covered everything?*

RM: We are finding is that the drugs are similar, but they are not identical. They have different targeting profiles. They have different pharmacodynamics and different safety profiles.

It's difficult to appreciate from looking at a list of approved drugs—but in patient management what we do is we sequence one drug after another, and what we find is that some patients benefit again and again from the sequenced agents.

For example, a patient may respond for a time period to sunitinib, and then when he progresses, we switch over to everolimus. The patient is treated with everolimus that until progression, and we switch over to sorafenib, and then maybe to bevacizumab. So what happens is that there is a population of patients who are managed for a very long time with these drugs sequenced one right after another.

This is an observation that oncologists who treat kidney cancer patients are experiencing in the clinic.

I care for kidney cancer patients who are alive for many years on these different drugs, and that is something I rarely saw before.

For example, there is a woman who comes to my clinic who was treated on one of the earliest clinical trials of temsirolimus, even before the trial used for FDA approval. Her treatment goes back more than 10 years, and she had a very bad case of kidney cancer. She has since been treated with nearly all the approved drugs, including sunitinib, sorafenib and everolimus, and her life has been extended dramatically.

We are seeing a tremendous benefit for the patients, just in terms of sequenced use, one target agent being given after another. I am not sure whether it is critical which one is given second-line or third-line, or vice-versa.

The main issue is that the patients get access to most or all of the medications at some time in their clinical course.

Bioinformatics

caBIG Leader Buetow Resigns; Will Announce New Job Later

(Continued from page 1)

including Booz Allen Hamilton and SAIC, and using as much as $350 million in appropriated NCI money, augmented by funds from the American Recovery and Reinvestment Act to build the cancer Biomedical Informatics Grid, abbreviated as caBIG.

Buetow's programs were curtailed by current NCI Director Harold Varmus, who initiated a review of caBIG, which, critics said, produced many unneeded, unusable, and buggy tools. caBIG was recently trimmed to $33.3 million, and all of its programs are under review by a subcommittee of the NCI Board of Scientific Advisors (The Cancer Letter, Dec. 2).

The email Buetow sent to NCI staff announcing his resignation Dec. 13 follows:

To the Cancer Community,

I'm writing to announce I will be leaving the National Cancer Institute to assume a new position.

This is an exceptional time in biomedicine, during which scientific and technological change is transforming everything in life sciences and health care. There could be no more exciting period in which to explore the new concepts and new models at the edge of what is feasible today and where we can see new light on the horizon.

During my 13-year tenure in government I have

attempted to work at that cutting edge. It has been my privilege to lead an NCI research laboratory with some of the world's most talented scientists, to work hand in hand with innovators across the cancer research community in designing and building a first generation national infrastructure for cancer studies, and to collaborate with the hugely dedicated staff of the NCI.

I could not have wished for more thoughtful colleagues, and I want to thank everyone for the work they do and the immensely meaningful chance to work alongside them over these years. I offer special heartfelt appreciation to the staff of the NCI's Center for Biomedical Informatics and Information Technology and its partners, who labor tirelessly behind the scenes as unsung heroes of the research enterprise.

My years at the NCI have been the most deeply fulfilling of my career, and my commitment to the fight against cancer remains undiminished. I wish all my NCI colleagues the greatest success in all their endeavors, and hope to find opportunities to enhance each other,s scientific work in my new environment.

I will be sharing the details of my next challenge shortly. In the meantime, my best wishes to everyone for a happy holiday season and wonderful New Year.

Sincerely,

Ken Buetow

Anil Potti Explains

Potti: MD Anderson "Rivals" Took Advantage Of CV "Mistake"

(Continued from page 1)

The Rhodes credential was a part of applications Potti used to obtain substantial funds from NCI, the Department of Defense and the American Cancer Society.

Potti attributed his troubles to what he describes as a rivalry between the Duke genomic researchers and scientists at MD Anderson Cancer Center. The problems in Potti's biography, including the Rhodes claim, were uncovered by this publication (The Cancer Letter, July 16, 2010).

In the letter to the South Carolina licensure board, Potti claimed that an earlier Duke internal investigation found the discrepancies in his CV and bios to be honest errors and claims that his science and patient care were solid. However, Potti's key papers have been retracted by the world's leading journals; the North Carolina Medical Board has reprimanded him for misstating his credentials; and Duke has settled 11 malpractice claims stemming from clinical trials involving his technology.

Also, Duke officials are conducting a scientific misconduct investigation focused on Potti. His statement that an earlier investigation had described his misstatement as a series of honest mistakes is incorrect, university officials said.

Finally, a one-time Potti supporter, Jeffrey Crawford, the George Barth Geller Professor for Research in Cancer and chief of medical oncology at Duke, recently told The Cancer Letter that he regretted writing Potti a letter of recommendation without knowing all the details surrounding his case (The Cancer Letter, Dec. 9).

The text of Potti's explanation follows:

January 20, 2011

Dear Chairman and the Members of the Board:

I am not sure if this was needed with my application for a South Carolina license, but I feel the need to provide some clarification with regards to a past controversy during my time at Duke University. While these issues were in no way related to my abilities, performance or conduct as a physician or care giver, I am writing this letter because I want to [be] completely transparent and shed some light on this. Thank you for taking the time to review and I apologize if this is irrelevant or redundant in any way.

Below, I have addressed the 'issues' with regards to my "Rhodes Scholarship" that led to an investigation by Duke University so that you all my have a chance to read this in detail and ask any further questions, if needed.

In 1995, while completing medical school training in India, I was nominated for a "Rhodes Scholarship from the Australian Board". After a series of interviews, I was notified (have evidence in the form of letter from the Ministry of Defense in India, one that Duke was able to obtain during its investigation) and congratulated on being the nominee from India. Being proud of this achievement I added this on to my resume/CV as 'Rhodes Scholarship (Australian Board)' and that carried over to some of my subsequent CVs. To be honest, coming from India, I did not know this was not the real Rhodes Scholarship (where people go to Oxford for additional training), but instead is a scholarship awarded by the Australian Association of Rhodes Scholars to meritorious students from commonwealth countries (like India)—another fact that was verified by Duke during their investigation which ultimately concluded that while the discrepancies were of concern, they were "honest errors" and DID NOT constitute scientific misconduct. (These reports are meant to be confidential to the institution UNLESS there was indeed evidence of misconduct found and I would appreciate it if you could

handle this information in a confidential manner as well).

I want to further clarify that in my appointment CV to Duke and later on, when I was up for promotion, I DID NOT reference the Rhodes. Likewise, my credentialing paperwork and application for hospital privileges at Duke Medical Center were NOT affected. Also, in 2007, once I became aware of that what was on some of my CVs (i.e. "Rhodes Scholarship (Australian Board)") was [in fact] very different from what is traditionally considered to be a Rhodes Scholar and this could be misleading, I removed it from all my CVs and resumes promptly. Also of note, there were several other more relevant (to patient care) and possibly more prestigious awards that I had received (ASCO awards, Humanism in Medicine award, Mentoring awards, etc.) that I had never referenced on any CV. Please understand that I am not trying to make excuses, I will be the first to admit that I made a mistake but only hope that you will see that it was an unintentional mistake and never done to gain unfair advantage.

Unfortunately, this Rhodes issue became a focal point for a larger controversy in the field of basic science genomics that had been looming for the past four-plus years between two academic rival groups at Duke University (which I was a part of) and MD Anderson Cancer Center and was played out extensively in the media. While no one in the scientific arena suggested any form of research misconduct, as part of due diligence after the Rhodes issue arose, Duke launched two evaluations:

1. A comprehensive review of my clinical practice—which as you can see revealed no issues of concern, based on the accompanying letter from Dr. Jeffery Crawford (Chief of Medical Oncology at Duke University Medical Center, addressed to my prospective employer in South Carolina), and

2. An evaluation in to the basic science genomics research and experimental data around research papers published and research grants obtained by several senior and junior faculty (including me) in the genomics program at Duke. This preclinical basic research work was performed on the undergraduate campuses at Duke and not in any way directly related to patient care. I am told that this evaluation will take 2-3 years to complete. It is important to note that during all of this, there were never any questions or concerns raised regarding the care I provided to my patients or the support offered to their families. Once again, I believe that the statements in Dr. Crawford's letter should help clarify that.

Although, as you might expect, some of this is embarrassing for me to admit. I am a honest man who believes in providing the best care for his patients and I will be the first to admit that I made a mistake a long time ago with regards to material on some of my CV, an unintentional naïve one, but a mistake nonetheless. Thus, I took responsibility for that mistake and resigned from Duke University. I am now very much looking forward to completely dedicating myself to patient care and diligently pursuing the reason I went to medical school in the first place – to provide empathetic care and help people.

I sincerely hope that this clarification has been helpful and I will be happy to answer any further questions, if needed.

Best regards,

Anil Potti

National Cancer Act, 40 Years Later

Senate Reaffirms Committment To Cancer Research Funding

By Conor Hale

Sens. Sherrod Brown (D-Ohio) and Jerry Moran (R-Kan.) introduced a Congressional resolution Dec. 13 commemorating the 40th anniversary of the National Cancer Act of 1971 and reiterated the federal government's commitment to funding cancer research.

The resolution—cosponsored by 43 other senators—pledges to maintain cancer research as a national priority, "to address the scope of this pressing public health concern."

The National Cancer Act was signed into law by President Richard Nixon Dec. 23, 1971. It is credited with beginning the War on Cancer and strengthening NCI's ability to coordinate a national research effort to find cures.

"Today, the National Cancer Institute and its parent agency, the National Institutes of Health, support critical research across the country, enhancing the work of universities, medical schools, teaching hospitals, private bioscience businesses and research institutions in every state," said Moran at a press event Dec. 13.

"This national commitment to research has saved millions of lives and billions of dollars."

"This year, more than 1.5 million Americans are expected to be diagnosed with cancer," said Brown. "One out of every three women and one out of every two men will develop cancer in their lifetimes."

"Today, 12 million cancer survivors are alive because of advances in the way we prevent, detect, diagnose, and treat cancer. And because of investments by the National Cancer Institute and NIH, critical cancer

research is being conducted across the country," said Brown.

The resolution was endorsed by more than 100 professional societies, advocacy organizations, universities, patient groups, hospitals and cancer institutes

"It is heartening to see senators from both sides of the aisle joining together to shine light on the urgent need to accelerate and strengthen the nation's efforts against the more than 200 diseases we know as cancer," said Margaret Foti, CEO of the American Association for Cancer Research.

"Today, more than any time in history, cancer researchers are maximizing the impact of the fundamental discoveries made over the past 40 years and are translating them into improved patient care," said AACR President Judy Garber. "Our ability to maintain this momentum depends upon a strong commitment by Congress to adequately fund the National Cancer Institute and its parent agency, the National Institutes of Health."

"Thanks to our nation's concerted effort to fight cancer, we've achieved substantial reductions in the cancer death rate and have pushed five-year survival rates for breast, testicular, and some childhood cancers to over 90 percent," said Allen Lichter, CEO of the American Society of Clinical Oncology. "The knowledge gained though NCI and NIH research on chemotherapy and targeted treatments, radiation therapy, surgical advances, and side effect management has improved care and helped achieve an 18 percent decrease in the cancer death rate since the 1990s."

"Cancer is no longer a virtual death sentence thanks to the significant progress we've made as a nation in the past 40 years," said John Seffrin, CEO of the American Cancer Society Cancer Action Network.

"However, this is no time to rest on our past success. We need to celebrate this historic milestone by redoubling our efforts, so we can find answers for the deadliest cancers that still elude us."

The text of the resolution follows:

A RESOLUTION recognizing the 40th anniversary of the National Cancer Act of 1971 and the more than 12,000,000 survivors of cancer alive today because of the commitment of the United States to cancer research and advances in cancer prevention, detection, diagnosis, and treatment.

Whereas 40 years ago, with the passage of the National Cancer Act of 1971 (Public Law 92–218; 85 Stat. 778), the leaders of the United States came together to set the country on a concerted course to conquer cancer through research;

Whereas the passage of the National Cancer Act of 1971 led to the establishment of the National Cancer Program, which significantly expanded the authorities and responsibilities of the National Cancer Institute, a component of the National Institutes of Health;

Whereas the term "cancer" refers to more than 200 diseases that collectively represent the leading cause of death for people in the United States under the age of 85, and the second leading cause of death for people in the United States overall;

Whereas cancer touches everyone, either through a direct, personal diagnosis or indirectly through the diagnosis of a family member or friend;

Whereas, in 2011, cancer remains one of the most pressing public health concerns in the United States, with more than 1,500,000 people in the United States expected to be diagnosed with cancer each year;

Whereas the National Institutes of Health estimated the overall cost of cancer to be greater than $260,000,000,000 in 2010 alone;

Whereas approximately 1 out of every 3 women and 1 out of every 2 men will develop cancer in their lifetimes, and more than 570,000 people in the United States will die from cancer this year, which is more than 1 person every minute and nearly 1 out of every 4 deaths;

Whereas the commitment of the United States to cancer research and biomedical science has enabled more than 12,000,000 people in the United States to survive cancer, 15 percent of whom were diagnosed 20 or more years ago, and has resulted in extraordinary progress being made against cancer, including—

(1) an increase in the average 5-year survival rate for all cancers combined to 68 percent for adults and 80 percent for children and adolescents, up from 50 percent and 52 percent, respectively, in 1971;

(2) average 5-year survival rates for breast and prostate cancers exceeding 90 percent;

(3) a decline in mortality due to colorectal cancer and prostate cancer; and

(4) from 1990 to 2007, a decline in the death rate from all cancers combined of 22 percent for men and 14 percent for women, resulting in nearly 900,000 fewer deaths during that period;

Whereas the driving force behind this progress has been support for the National Cancer Institute and its parent agency, the National Institutes of Health, which funds the work of more than 325,000 researchers and research personnel at more than 3,000 universities, medical schools, medical centers, teaching hospitals,

small businesses, and research institutions in every State;

Whereas the commitment of the United States to cancer research has yielded substantial returns in both research advances and lives saved, and it is estimated that every 1 percent decline in cancer mortality saves the economy of the United States $500,000,000,000 annually;

Whereas advancements in understanding the causes and mechanisms of cancer and improvements in the detection, diagnosis, treatment, and prevention of cancer have led to cures for many types of cancers and have converted other types of cancers into manageable chronic conditions;

Whereas continued support for clinical trials to evaluate the efficacy and therapeutic benefit of promising treatments for cancer is essential for translating new knowledge and discoveries into tangible benefits for patients, especially because all standard cancer therapies began as clinical trials;

Whereas, despite the significant progress that has been made in treating many cancers, there remain those cancers for which the mortality rate is extraordinarily high, including pancreatic, liver, lung, multiple myeloma, ovarian, esophageal, stomach, and brain cancers, which have a 5-year survival rate of less than 50 percent;

Whereas research advances concerning uncommon cancers, which pose unique treatment challenges, provide an opportunity for understanding the general properties of human cancers and curing uncommon cancers as well as more common cancers;

Whereas crucial developments have been achieved in cancer research that could provide breakthroughs necessary to address the increasing incidence of, and reduce deaths caused by, many forms of cancer;

Whereas research into the effect of certain forms of cancer on different population groups offers a significant opportunity to lessen the burden of the disease, because many population groups across the country suffer disproportionately from certain forms of cancer; and

Whereas a sustained commitment to the research of the National Institutes of Health and the National Cancer Institute is necessary to improve the entire spectrum of patient care, from cancer prevention, early detection, and diagnosis, to treatment and long-term survivorship, and to prevent research advances from being stalled or delayed: Now, therefore, be it

Resolved, That the Senate—

(1) recognizes the 40th anniversary of the National Cancer Act of 1971 (Public Law 92–218; 85 Stat. 778); and (2) celebrates and reaffirms the commitment embodied in the National Cancer Act of 1971, specifically, that support for cancer research continues to be a national priority to address the scope of this pressing public health concern.

In Brief

Fox Chase, Temple Health System Sign Affiliation Agreement

FOX CHASE Cancer Center and the **TEMPLE UNIVERSITY Health System** signed an affiliation agreement.

Fox Chase will expand its outpatient and surgical care services, and will lease space in the Temple-affiliated Jeanes Hospital, the cancer center's immediate neighbor in Philadelphia.

The agreement creates a 47.5-acre site that will serve as Temple's "cancer hub."

The affiliation also allows Jeanes to provide a broad array of services on its premises, including: outpatient diagnostic testing, interventional radiology, breast care, general surgery, thoracic surgery, endocrine surgery, urology and diagnostic GI.

The university's health system will also invest in cancer research at Fox Chase.

"We're always working to strengthen the center's ability to more vigorously pursue our mission to prevail over cancer, and we believe that this affiliation with Temple University Health System will do just that," said **Michael Seiden,** president and CEO of Fox Chase.

"[It enables] us to begin recruiting new researchers and clinicians almost immediately and to expand our clinical services significantly in coming years to serve the region's cancer-care needs well into the future."

YUSUKE NAKAMURA will step down from his position as head of the office promoting Japanese medical innovation within the prime minister's cabinet and move to the University of Chicago in April 2012.

The Tokyo University professor hopes to advance new anticancer drugs in the U.S. through genomic research. As Japan's leading researcher in genomics, Nakamura played a central role in the International Human Genome Project.

The cabinet office was launched in January. Koichi Tanaka, a Nobel laureate in chemistry, was appointed as one of its acting chiefs.

Then-Chief Cabinet Secretary Yoshito Sengoku hoped the office would lead efforts to strengthen the Japanese medical industry's competitiveness by

eliminating barriers among ministries and agencies.

However, Sengoku stepped down shortly after the office was launched, and no top cabinet officials attended the third meeting the office held in October.

Nakamura said he felt that Japan was powerless to develop new drugs, even though he had made efforts to change the system. "It was my dream to deliver new drugs developed in Japan to Japanese people first," he said. "As it was impossible here, I'd like to realize new drugs in the United States."

The Japanese government injected more than ¥1.6 trillion (approximately $20.4 billion) into life sciences from 2006 to 2010. However, the majority of innovative new anticancer drugs were developed outside of Japan.

THOMAS SMITH was appointed director of palliative care for **Johns Hopkins Medicine and the Sidney Kimmel Comprehensive Cancer Center**.

He will also hold the first Harry J. Duffey Family Professorship of Palliative Care in the department of oncology.

Smith previously served as the medical director of the Thomas Palliative Care Program and as the co-director of the Cancer Control and Prevention Program at Virginia Commonwealth University's Massey Cancer Center.

Smith focuses his research on neuropathic pain, end-of-life care and cost issues.

THE ROSWELL PARK CANCER INSTITUTE GENOME PROJECT was approved by New York State Governor Andrew Cuomo's Regional Economic Development Council initiative.

The project will compile and analyze the genomes of Western New York citizens.

The $5.1 million award will cover the project's two-year pilot phase, in which 1,000 area residents will be asked to donate a blood sample and provide detailed medical information. The project will examine genetic factors that play roles in cancer as well as diabetes and heart disease.

Roswell Park President and CEO **Donald Trump** and Deputy Director **Candace Johnson** will lead the genome project as co-investigators.

The institute will partner with the University at Buffalo, Kaleida Health, the Catholic Health System and Erie County Medical Center, HealthNow/Blue Cross Blue Shield, Independent Health, Univera Healthcare, The P2 Collaborative, and HEALTHeLINK.

STAND UP TO CANCER, the **MELANOMA RESEARCH ALLIANCE** and the **AMERICAN ASSOCIATION FOR CANCER RESEARCH** announced a new scientific dream team dedicated to melanoma research.

The SU2C-MRA Melanoma Dream Team Translational Cancer Research Grant provides $6 million over a three-year period. The project's goal is to accelerate the application of new therapeutic agents to the clinic.

Jeffrey Trent and **Patricia LoRusso** will lead the team project "Personalized Medicine for Patients with BRAF Wild-Type Cancer."

Trent is president and research director at the Translational Genomics Research Institute and head of the melanoma therapeutics lab. LoRusso is director of the Eisenberg Center for Experimental Therapeutics and professor of oncology at Karmanos Cancer Institute and Wayne State University School of Medicine. LoRusso will oversee all of the dream team's work in clinical trials.

Team members will molecularly profile BRAFwt and BRAF-mutant cell lines and test for sensitivity to 100 prioritized compounds that might translate into therapeutic utility.

Researchers will use these data to generate models that predict the sensitivity of BRAFwt melanomas to specific drugs. They will test these predictions using xenografts of the melanoma cell lines and primary tumors.

A clinical trial will determine whether this personalized approach significantly improves clinical outcome. The goal is a 30-percent improvement in tumor response relative to standard-of-care therapy. Clinical trials are expected to begin in mid-2012.

In addition to Trent and LoRusso, principal team members include: **Svetomir Markovic**, Mayo Clinic; **Brian Nickoloff**, Michigan State University; **Neal Rosen**, Memorial Sloan-Kettering Cancer Center; **Nicholas Schork**, The Scripps Research Institute; **Aleksandar Sekulic**, Mayo Clinic; **Jeffrey Sosman**, Vanderbilt University; **Kristiina Vuori**, Sanford-Burnham Medical Research Institute; **Craig Webb**, Van Andel Research Institute; and **Joshua LaBaer**, The Biodesign Institute at Arizona State University;

The team also includes advocates **Mark Gorman**, National Coalition for Cancer Survivorship; **Derrick Hall**, president of the Arizona Diamondbacks; retired Florida **Sen. Connie Mack**; and **Jane Perlmutter**, Gemini Group.