



## A "Proton Bubble"

### **Indiana to Close Proton Beam Facility Amid Nationwide Building Boom**

*By Matthew Bin Han Ong*

At its opening a decade ago, the Indiana University Health Proton Therapy Center was one of four such facilities in the U.S.

Alas, money woes struck immediately. The center has run at a deficit for most of its existence—recently losing over \$3.5 million in operating costs in fiscal 2013. And now the center is a landmark once again: On Jan. 1, 2015, it will become the first proton beam center in the U.S. to be closed.

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## Conversation with The Cancer Letter

### **IU's Loehrer Discusses "Business Decision" To Close Bloomington Proton Beam Center**

The Cancer Letter asked Patrick Loehrer, director of the Indiana University Melvin & Bren Simon Cancer Center, to discuss his institution's decision to close its 10-year-old proton beam center.

No other institution in the U.S. has closed such a facility.

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## Genentech Reps Not Welcome

### **Hospitals Urge Drug Maker to Reverse Policy On Supplying Avastin, Rituxan, & Herceptin**

*By Paul Goldberg*

Cancer centers and other hospitals, reeling from the loss of discounts and rebates on three widely used cancer drugs, are seeking to persuade drug maker Genentech to reverse its decision to channel these medications through six specialty distributors.

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## Committee Unanimously Recommended Closing

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“Predominantly this was a business decision,” said Patrick Loehrer, director of the Indiana University Melvin & Bren Simon Cancer Center, who served on a committee that recommended closing the facility. “The other factor had to be geographic, by the way. From a translational research component, to have a facility that is an hour away [from the Indianapolis-based cancer center] was not ideal.”

A conversation with Loehrer appears on page one.

The final phase of the Bloomington-based center is all the more remarkable because it’s playing out against the backdrop of a nationwide building boom of such centers.

The center will be shut down pursuant to recommendation from an independent review committee that concluded that an upgrade would require significant investment, and would not decrease costs sufficiently to enable the center to break even.

But money and distance were not the only issues.

In its unanimous recommendation to close the center, the six-member panel cited growing competition, falling reimbursement rates, and the lack of conclusive evidence for superior safety and efficacy of proton beam therapy over conventional radiation therapy.

“[Investigators have failed] to demonstrate in a scientifically robust fashion the putative benefits of this therapy,” the committee wrote. “There have, to date, been no completed randomized trials at any site demonstrating ‘proof of principle.’”

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“There have been very few prospective quality-of-life studies documenting advantage, even in children. Proton beam does not, therefore, feature in most national guidelines for cancer care.”

A copy of the committee report was obtained by The Cancer Letter, and is posted [here](#).

According to the committee, there are 15 centers in operation in the U.S., with at least 20 more in the construction or planning stages. A larger facility can cost up to \$200 million to build. A smaller one-room unit can cost about \$30 million.

In the Washington, D.C.-Baltimore region alone, three centers are being built in close proximity to each other. When completed, the centers—located at the University of Maryland, Georgetown University Hospital, and Sibley Memorial Hospital—will have a combined capacity of treating 3,225 patients per year (The Cancer Letter, [Oct. 25, 2013](#)).

“Indiana University clearly has some issues that are unique to their situation, based on the facility and how it was designed and built,” said Kevin Cullen, director of the University of Maryland Marlene and Stewart Greenebaum Cancer Center. “However, their report raises a lot of important questions that are applicable to the oncology community and the radiation oncology community in general, that I think led them to this very difficult situation.

“A lot of factors that the committee cites are relevant to centers anywhere in the country.”

Formed by Jay Hess, vice-president for university clinical affairs and dean of the IU School of Medicine, the review committee consisted of:

Committee chair **Theodore Lawrence**, the Isadore Lampe Professor and chair of the University of Michigan Cancer Center Department of Radiation Oncology;

**Stephen Hahn**, chair of the University of Pennsylvania Department of Radiation Oncology, director of the Photodynamic Therapy Program, and co-program leader of radiation biology;

**Patrick Loehrer**, associate dean for cancer research, director of the Indiana University Melvin & Bren Simon Cancer Center, associate director of clinical research, and H. H. Gregg senior professor of oncology;

**Dennis Murphy**, chief operating officer of Indiana University Health;

**Anthony Zietman**, associate director of the Harvard University Radiation Oncology Residency Program at the Massachusetts General Hospital, and Jenot W. and William U. Shipley Professor of radiation oncology at Harvard Medical School; and

**Ellen Burton**, university clinical affairs program

manager at Indiana University.

“We were given a number of charges,” Loehrer said to *The Cancer Letter*. “First and foremost was basically whether or not this facility’s model is financially feasible, and whether or not this is something that the health care system needs, going forward. We also assessed the status of proton therapy, and whether or not it is critical to the mission of the IU Simon Cancer Center and IU Health.”

Minesh Mehta, medical director of the University of Maryland Proton Treatment Center, said the IU decision is understandable.

“I don’t think the closure is surprising, that they made the decision that their facility has gotten to a point of obsolescence,” Mehta said to *The Cancer Letter*. “Rather than being an isolated event, because you can probably find one factor or more that are relevant, IU was probably caught in a situation analogous to a perfect storm, where all of the factors came together.”

The Bloomington facility now faces competition from newer centers in nearby metropolitan areas.

“For instance, the center in Chicago that now exists, was not there when the Bloomington center was built,” Mehta said. “IU probably had patients coming in from the Chicago area in the past, and presumably those patients are now getting their care in Chicago. St. Louis has also opened a proton therapy center, and those patients would no longer be coming in to Bloomington.”

### **Conventional Therapies Catching Up**

Conventional radiation therapies and alternative treatment options to proton beam have improved, the review committee wrote, adding that those advances were important considerations in deciding the fate of the Bloomington facility.

“Photon beam (i.e. standard) radiation therapy did not stand still, and ‘intensity-modulated’ techniques (which can turn one beam into hundreds of ‘beamlets’) of external radiation or stereotactic radiation therapy (which uses many relatively low intensity beams focused on the tumor, thus producing an ablative treatment with little toxicity) have closed the gap with proton beam to an unanticipated degree,” the committee wrote.

Loehrer said the scientific value of proton therapy in comparison to conventional therapies was a factor in IU’s decision.

“When one compares proton therapy to historical data on photon therapy, it’s clear that proton therapy comes way ahead,” Loehrer said to *The Cancer Letter*. “However, there’s been evolution in how photon therapy is now delivered including stereotactic radiotherapy

and IMRT. These modalities come much closer to the advantages from normal tissue damage seen with proton therapy at the present time.

“The other concern is that randomized trials comparing photon vs. proton have not been completed. There have been a couple trials that have been initiated, and I do look forward to the completion of those trials. I will be particularly interested in potential long-term side effects of protons, and assurances that there are no other side effects that we believe many [patients] develop.”

Trials comparing proton and conventional therapies are underway, said Walter Curran, chair of the Department of Radiation Oncology at Emory University, director of the Winship Cancer Institute, and a co-chair of NRG Oncology, a group within the new NCI-supported National Clinical Trials Network.

“At the moment, we’re conducting a phase III trial comparing proton therapy with chemotherapy to intensity-modulated radiation therapy with chemotherapy for patients with stage III non-small cell lung cancer,” Curran said to *The Cancer Letter*. “We’re about to activate a study evaluating proton therapy vs. IMRT with chemotherapy for patients with glioblastoma multiforme and having a number of other studies evaluating proton therapy for patients with other malignancies—like, would it be open within NRG Oncology over the next few years.”

The Emory Winship Cancer Institute in Atlanta is constructing a five-room proton beam center, similar to the upcoming University of Maryland facility in Baltimore. Both institutions are partnering with a private company, Advanced Particle Therapy, LLC of San Diego.

“There’s a lot of emerging data that points to a clear clinical benefit in many other disease sites, and some of these data is already reported, some of it is already out there, and I think we’ll see more and more over the next few years,” Curran said. “There’s very interesting new data suggesting decreased toxicity for patients receiving such treatment for head-neck cancer, lung cancer, and potential benefit in liver tumors.”

There are benefits in using proton beam therapy for the treatment of pediatric and eye and skull-base tumors, but those benefits are, for now, largely limited to those sites, IU’s review committee wrote.

“At present, we can say that there are sites where a clinically meaningful advantage likely exists, those where it likely does not exist (most breast or GI cancers), and those where it needs formal investigation (liver and lung),” the committee wrote. “The future of proton therapy will depend in part upon the demonstration of

a meaningful clinical advantage in some, any, or all of these clinical sites, and in part on technological advances that will allow it to ‘pull away’ from the competition once again.”

Maryland’s Cullen agrees.

“I think there is certainly the strongest evidence for use in those sites,” Cullen said to *The Cancer Letter*. “But it will be awhile before we know for certain how much benefit proton therapy will have compared to photon for other diseases at other sites.”

It will take large-scale collaborations to achieve those results, said Emory’s Curran.

“Until there is sufficient critical mass of centers with the very latest technology, until these centers really come together and do prospective research, it’s difficult to say that the benefit is less limited to these [pediatric, eye, and skull-base] tumors,” Curran said. “As the data emerge, it appears that the benefit’s going to be extending to more and more types of cancer, but it does require discipline on the part of the centers, which will have this technology, to systematically study it.

“That’s already happening at a number of centers that are open, and I’m quite certain that will also happen at the University of Maryland center as well as the Winship center in Atlanta.”

These collaborations will be difficult to put together, as many facilities will individually compete for the same patient populations, Cullen said.

“I personally think that there is a need to collaborate on the kind of research studies that will answer those questions as quickly as possible, and unfortunately, when multiple sites are building facilities in close proximity, it’s going to make that kind of important research harder to complete,” Cullen said.

### **The Question of Demand**

The IU review committee pondered at length the survival of existing proton therapy facilities.

“It is quite possible that we are on the verge of a ‘proton bubble,’ with the more indebted centers or those without a strong patient supply line closing,” the committee wrote. “Those with less or no debt, or those built around academic institutions, will likely survive and continue to provide the care that pediatric and base of skull tumor patients need. It is hoped that they will develop the data necessary to define the exact role of proton beam therapy in oncology.”

Projected patient volume and revenue targets in Bloomington didn’t justify new investment in the center.

“These [targets] seem very difficult to achieve given the current proposed development of over 30 new

facilities, particularly in current key referral markets like Ohio (Ohio State University) and Minnesota (The Mayo Clinic) where this facility draws the majority of its out of state referrals, and declining payer reimbursement rates,” the committee wrote.

Loehrer said he wonders whether many proton facilities are being built for marketing advantage.

“I would also have concerns that there is not much need assessment done for the country in terms of facilities,” Loehrer said. “How many do we need, and where should they be located to best serve our patients?”

Cullen said the U.S. is building far too many proton therapy centers.

“I think that there is the real risk that we are seeing, and will see, a ‘proton bubble’—as they described it—and I think it makes me feel more strongly that centers should really, wherever possible, collaborate and consolidate their efforts to develop and invest in these facilities,” Cullen said. “Otherwise, we’re going to have much more capacity than is justified, and ultimately, that’s going to be an unsustainable expense for the centers that are building these facilities.”

Cullen predicts vigorous competition for patients in the D.C.-Baltimore area.

“I’ve looked at the business plans for all three facilities as part of the District of Columbia certificate of need process—and I think it’s fair to say that all of them are very optimistic and don’t really take into significant account the possibility that additional facilities will be built in the immediate area,” Cullen said.

“It’s inconceivable to me that the three facilities will achieve their business projections, and if there are three facilities open in a small area, it seems very likely that none of them will meet their original volume projections.

“But Hopkins and MedStar had said, no, they don’t want to do it, they want to build their own.

“I’m very puzzled by the decision making at MedStar and Hopkins that makes them want to continue to develop their facilities independently given all of the economic issues that the closure of Indiana raised.”

The conclusion that there would be a capacity overload for proton beam therapy in the U.S. may be too simplistic, said Mehta, medical director of the University of Maryland center, which will have a capacity of treating 2,000 patients annually when all five rooms are completed in late 2016.

The center will be run by the Department of Radiation Oncology, which does not report to Cullen or the Greenebaum Cancer Center. No funds from the cancer center or the university is involved in the

construction or maintenance of the proton facility, Cullen said.

“The assumption that the capacity has been exceeded implies that these so-called experts have a clear definition, in their minds, as to what the capacity is, and what represents excess capacity,” Mehta said. “And so the implications of that assumption would be, that I, as this expert—and I’m merely paraphrasing—although I’ve never actually used proton therapy myself, I’m somehow enough of an expert to know exactly what’s going to happen with proton therapy in the next three, four, five or 10 years, and can predict with precision, how many patients will benefit, and I can therefore give you a capacity rate, and tell you what the capacity is.

“You can very well imagine that there are so many assumptions in a scenario like that, that the likelihood that such a statement would be true is low.

“Believing that would be quite simplistic.”

## Conversation with The Cancer Letter **Loehrer: Decision to Close Center Was "Heartbreaking"**

(Continued from page 1)

Loehrer spoke with Matthew Ong, a reporter with The Cancer Letter.

**Matthew Ong:** *Why did Indiana University decide to close the proton beam facility at Bloomington?*

**Patrick Loehrer:** Well, predominantly this was a business decision. We did not think, moving forward, that it would meet the needs of the future of our health care system and cancer center both economically and for research growth.

**MO:** *Are there any lessons, implications or conclusions that other centers and facilities should draw from IU's decision to close its facility?*

**PL:** This is a very unique situation, because this facility was one of the first four proton facilities in the country, and it was generated as a way to save an aging physics program down in Bloomington. That program was modified to construct a proton beam center, and they did an incredible job of engineering this facility.

But it became obvious that the upkeep and renovation of this would still not make it comparable to some of the more modern proton facilities that are currently being built.

**MO:** *I see from the review committee's report that a major factor was the sizable investment needed to upgrade the technology. Were there other considerations?*

**PL:** The other factor had to be geographic, by the

way. The proton facility is south of Indianapolis, which is where the hub of the IU Simon Cancer Center exists, and where the bulk of our clinical and translational research is housed. Our children's hospital—the largest facility for the state—is in Indianapolis, and our phase I program is here, so from a translational research component, to have a facility that is an hour away was not ideal. That was a large factor in this decision.

**MO:** *What about scientific factors?*

**PL:** We had a very well-recognized and thoughtful review committee that was led by Ted Lawrence from the University of Michigan, with Steve Hahn from the University of Pennsylvania, and Anthony Zietman from Massachusetts General. In addition there was Dennis Murphy, who is the chief operating officer from IU Health, and myself, serving on the committee.

We were given a number of charges.

First and foremost was to determine whether or not this facility's model was financially feasible, and whether or not this is something that the health care system needs, going forward. We also assessed the status of proton therapy, and whether or not it is critical to the mission of the IU Simon Cancer Center and IU Health.

The scientific value of proton therapy certainly was discussed in general, and I think it has major implications in cancer care, but it was not the principal component of this decision. This particular discussion will factor into further discussions about whether or not IU Health will invest in proton facilities in Indianapolis at the IU Simon Cancer Center.

**MO:** *Can you discuss those scientific implications as well?*

**PL:** This has been well outlined. In fact, there was a recent issue in the Journal of Clinical Oncology in which Anthony Zietman was a co-author on a paper, and I thought he did an excellent job with this. There was also a very thoughtful analysis of this which also contained a number of quotes from Anthony in a recent issue of Discover Magazine.

When one compares proton therapy to historical data on photon therapy, it's clear that proton therapy comes way ahead. However, there's been evolution in how photon therapy is now delivered including stereotactic radiotherapy and IMRT. These modalities come much closer to the advantages from normal tissue damage seen with proton therapy at the present time.

The other concern is that randomized trials comparing photon vs. proton have not been completed. There have been a couple trials that have been initiated, and I do look forward to the completion of those trials. I will be particularly interested in potential long-term

side effects of protons, and assurances that there are no other side effects that we believe many develop.

**MO:** *What was IU's process in approaching this problem? How was the review committee formed, and how were the members, including you, chosen?*

**PL:** This was under the charge of the dean of the IU School of Medicine, Jay Hess, who selected the members. I was not part of the process of how he selected each of us, but he did bring two members from institutions that already have proton facilities (Hahn and Zietman). Ted Lawrence was past president of ASTRO, and a very well thought of radiation oncologist who also has a background in medical oncology. Also, Jay knows him from his time at the University of Michigan.

And, obviously me, because I'm the director of the Simon Cancer Center, and Dennis Murphy was a logical choice because IU Health has a lot of skin in the game for this facility.

**MO:** *You were saying that the facility was built in Bloomington in the first place, as opposed to in Indianapolis, because of the physics department?*

**PL:** The Indiana University had a very strong physics department—and still does—and this was, as funding for that cyclotron was declining, it was a thought process that perhaps this could be converted to therapeutic value, and so this was converted back a decade ago now, in 2004.

This was initially an investment of Indiana University-Bloomington, which established a freestanding clinic. Eventually, IU Health became an investor in the Proton Therapy Center and then became part of the IU Health system. But behind it, there still was—if you will—debt that was accrued for the renovations of the buildings and clinical facilities in this somewhat isolated Bloomington facility.

**MO:** *Is IU the first to close a proton beam center in the U.S.? Do you know who is next?*

**PL:** I'm not aware of anyone else closing a proton facility, so we probably are the first one to do this.

**MO:** *What's it like to be the first cancer center director to shut down a proton beam facility in the U.S.?*

**PL:** I enjoy my job. But this was a very difficult decision, and not just for the closure of the facility, but because there are incredible staff that are working down in Bloomington that have spent a decade serving patients and working to keep this facility going.

That is extremely difficult, and in many ways, heartbreaking to do this for our staff and faculty, but economically this is a tough decision, and particularly, when we think about value-based therapy in these tough economic times, we had to make a hard decision, and

this decision was made.

**MO:** *What kind of patients was the Bloomington facility treating?*

**PL:** There were a number of pediatric tumors that came down there. Probably a third of head and neck patients, particularly with base of skull tumors. Brain tumors represented about a third of the patients that were there. Prostate cancer, which I know is common to many different centers, was about 18 percent.

**MO:** *So in the broader economic view of this issue, the committee report also says that there is a growing "proton bubble." Is there? Does capacity exceed need?*

**PL:** I do personally have some concerns about whether or not proton facilities are being built for, in many ways, marketing advantages. I would also have concerns that there is not much need assessment done for the country in terms of facilities. How many do we need, and where should they be located to best serve our patients?

I do think in times of economic crisis right now, it is up to us to make some very tough decisions about how we expend our health care dollars. And I think this is one decision that we made here. I think other health care systems would benefit from making similar thoughtful analysis of high expenditure items.

**MO:** *In view of all that, and since IU says the Bloomington facility has been losing money for most of its existence, are proton beam therapy centers economically viable in most places? Can people make money off these things, as far as we can see?*

**PL:** Well, our advisors in Boston and Philadelphia tell us that they are making money on their proton facilities; at least this is how they explained it to us. But there is a carry-over effect. They get more referrals for consideration of proton therapy, and many of them go on to receive radiation therapy via the conventional route, or through stereotactic radiotherapy.

So by having this facility, many times it attracts patients there, so they believe that it is useful that way. And I believe that many other centers are setting it up that way.

I believe, as time goes on, there is a real concern whether or not the reimbursement for proton therapy is sustainable. Some of the profits that are currently seen may not be as strong down the road.

So one needs to thoughtfully think about an investment of \$20 to \$30 million, whether or not you can justify that for your health care system, but, more importantly, how this expense is spread across the patients.

**MO:** *Advocates say that emerging data and further research appear to show greater and broader*

*application for the use of proton therapy in other types of tumors. Is that promise worth investing in again for IU at any point in the future?*

**PL:** I strongly believe that we are going to readdress this issue at IU, and I think for us, if we do invest in a proton facility, it will be closer to our main base of operations and our pediatric hospital. I believe we would also focus on how to better define the optimal populations for proton therapy and novel combined modality approaches such as chemo-radiotherapy through our phase I program with photon therapy, as well as looking at the impact upon survivorship issues.

The greatest apparent benefit for proton therapy appears to be in the pediatric population, and because we have such a strong pediatric cancer research program here, we will have to think about this very strongly in terms of its potential usefulness.

But we are not in favor of doing it just to keep up with another health care system.

**MO:** *Is it true that the only clinically meaningful advantage, thus far, of proton beam therapy is limited to pediatrics, and for treatment of eye and skull base tumors?*

**PL:** Ideally, you'd want to minimize toxicity to any normal tissue in the body when you give radiation, and proton therapy, as how it's designed and theoretically working, should do that. But in particularly sensitive parts of the body, the anatomy would really preclude us from wanting to radiate very sensitive areas.

In other areas of the body, the body will be a bit more forgiving. And so a wider area—in the liver, for example—the liver can compensate for that. A wider area that would include the spinal cord, or the medulla oblongata is not going to be as tolerant to this.

So I think there are particular areas of very high impact for protons, and there are other areas that I think the differences between conventional therapy and proton therapy are going to be minimized.

**MO:** *Would this be a right time to sell you a carbon ion gizmo?*

**PL:** Yeah, no comment.

**MO:** *Is there anything we've missed?*

**PL:** The last thing I'd like to say is that we take no great joy in closing down any facilities. I think this was a thoughtful process, and I have great pride in the staff and the faculty who have been involved with this facility over the past decade.

We have done some very unique research down there, but I think as we move forward, all our therapeutic modalities, whatever they are, I do think we need to do this kind of very careful analysis of the benefit and value for the patients and for the health care system.

## Genentech Reps Not Welcome **NCCN Urges Change in Policy; Moffitt, Ascension Ban Sales Reps**

(Continued from page 1)

Until Oct. 1, Avastin (bevacizumab), Herceptin (trastuzumab) and Rituxan (rituximab) could be ordered from wholesalers, which provided discounts and rebates on large purchases (The Cancer Letter, [Oct. 3](#)). Genentech is a unit of Roche.

The company's switch to specialty distributors, in effect, eliminated these benefits.

In protest, Moffitt Cancer Center and Ascension, a Catholic health system that operates 1,900 sites of care nationwide, said separately that they would no longer allow Genentech sales reps to enter their facilities. At least two other cancer centers and one consortium of centers are in the process of instituting similar restrictions, The Cancer Letter has learned.

In another reaction, the National Comprehensive Cancer Network urged Genentech to reconsider the shift that eliminated discounts on nearly \$8 billion worth of drugs almost overnight. Industry insiders estimate that the loss of rebates and discounts on these drugs could cost hospitals an estimated \$300 million.

"On behalf of our 25 leading cancer centers, NCCN urges you to reconsider this unfortunate decision," NCCN CEO Robert Carlson wrote to Genentech CEO Ian Clark. "Please continue to distribute bevacizumab, trastuzumab, and rituximab through the traditional distribution channels."

According to the IMS Health National Sales Perspectives, U.S. sales of Rituxan topped \$3.3 billion in 2013; Avastin amounted to \$2.7 billion; and Herceptin made \$1.9 billion. The prices are tracked on the wholesale level.

Genentech's decision bypasses more than 80 full-line wholesale drug distribution centers, requiring hospitals to order from facilities operated by the specialty distributors, which usually means relying on express courier shipments. The change affects only hospital pharmacies. Office-based oncology practices have been purchasing drugs exclusively from specialty distributors for decades.

The company said its objective is to enhance efficiency and security of the supply chain for these widely used medications. Genentech spokeswoman Charlotte Arnold said the controversy hasn't disrupted availability of the drugs in question.

"Patients are our primary concern, and we believe patients are still getting the medicines they need,"

Arnold said to The Cancer Letter. “Our relationships with our customers are extremely important to us.”

The company’s distribution model remains unchanged, Arnold said. “We believe this distribution model best serves patient safety and access and will continue to work with hospitals on this change,” she said. “We believe it is important for us to engage with doctors to share information about our medicines. When doctors are better informed about the benefits, risks and appropriate uses of medicines, patients benefit from better care.”

Independently of this controversy, some institutions have imposed uniform restrictions on all pharma company access to their facilities. For example, [a 2012 policy](#) at Memorial Sloan Kettering Cancer Center restricts industry reps in the following manner:

“Industry representatives may be present at an MSKCC meeting only if invited by MSKCC staff. There must be a bona fide scientific, educational, or business purpose that serves MSKCC’s interests for the industry representative to be present. Examples of situations in which it is permissible for industry representatives to be on site include:

1. “Inservice for MSKCC Staff for training on a new drug, device or equipment.
2. “Evaluation of new devices or equipment.
3. “Attendance at grand rounds, as long as the representative is present only as an audience member.”

### **Genentech Reps Barred from Moffitt, Ascension**

In a letter to Genentech, Gene Wetzstein, director of Pharmacy Services at Moffitt Cancer Center, said the company’s sales, marketing and corporate personnel would not be allowed on campus until the matter is resolved.

*The text of Wetzstein’s letter follows:*

I have discussed with MCC executive leadership and as an organization we are very displeased and discouraged with this decision and the negative impact that it will have on our organization and our patients.

As we discussed and as Genentech is well aware, this will result in a substantial negative financial impact that will exceed \$1.2M to MCC alone. In addition, operationally, this will be a step backwards with respect to efficiency, timeliness, and analytics.

It is also important to reiterate that these products have been distributed through regular channels (primary wholesalers) for many years (Rituxan 1997; Herceptin 1998; Avastin 2004) without issue.

If Genentech’s concern is truly the safety and the integrity of their medicines as the letter states,

then it would be a great opportunity for Genentech to partner with organizations like ours to provide this safety/integrity enhancement with no negative financial implications to our organization. It is unfortunate that at a time when we are working closely with manufacturers to assess how we can better partner with them, Genentech takes the above stance.

We have partnered with Genentech in clinical trials to bring these products to market. We certainly support patient safety and high quality. We also support efficient and affordable access to these medications for both patients and providers. Burdening providers of \$300 million globally will make it even more difficult for all of us to meet our community and patient needs.

We fully support the position of other facilities and organizations (ADCC, HOPA, etc.) and strongly recommend Genentech reconsider this decision. With that said, effective immediately all Genentech sales/marketing/corporate personnel will no longer have access to Moffitt Cancer Center until the above issue is satisfactorily addressed. In addition, any potential partnership discussions between MCC and Genentech will be placed on hold.

We understand the economics are challenging for all stakeholders including Genentech and we are willing to work collaboratively with you to identify a mutually agreeable option that ensures safety, access, affordability and patient satisfaction.

### **Ascension’s Letter**

*The text of the letter from Roy Guharoy, vice president of clinical integration and chief pharmacy officer at Ascension Health, and Michael Gray, the health system’s vice president and chief strategy officer, follows:*

Effective immediately all Genentech sales representatives are no longer allowed access to Ascension facilities. All Genentech sales representatives have been red lighted in our vendor credentialing system.

This move is based upon recent changes in Genentech business strategies that are not in the best interest of Ascension, our communities or the poor and vulnerable we serve. This action, combined with Genentech’s choice to not contract for cost relief on any of their products, reduces the dollars needed to provide the breadth of care important to our communities.

Genentech embarked on a business strategy to re-classify three of its oncology drugs as “specialty drugs.” As a result of the decision to change its distribution system, Genentech’s use of specialty distributors is resulting in unprecedented price hikes,



the results of which will harm the patients we serve.

Medication costs are increasing, particularly those identified as “specialty drugs,” and this is only going to become more critical in the coming years. One estimate notes that by 2020, spending on specialty drugs will quadruple from \$87 billion to more than \$400 billion. In 1990, there were only 10 specialty drugs on the market.

In 2012 there were nearly 300 drugs that were classified as a specialty drug. Yet, there is no industry standard definition for what constitutes a specialty drug. Current definitions allow a drug to be classified as a specialty drug for a wide range of reasons including the following: treatment cost greater than \$600 a month, treatment of a rare condition, requires special handling, use of limited distribution network, or requires ongoing clinical assessment. Thus, most all medications may be identified as “specialty” if desired by a manufacturer.

The end result is large price hikes—unaccounted for in our FY2015 budgets—and will mean that already scarce resources will need to be stretched with potential serious impact on the range and breadth of health services we currently provide to our patients and our communities.

[The letter](#) from the Hematology/Oncology Pharmacy Association (HOPA) to the Genentech CEO of North American Operations summarizes the negative impact Genentech’s decisions are having on the healthcare industry. Other national organizations are also mobilizing efforts to address the impact of these negative changes.

#### **NCCN’s Letter**

*The text of NCCN CEO Robert Carlson’s letter to Genentech follows:*

The National Comprehensive Cancer Network, an alliance of 25 of the world’s leading cancer centers, is extremely concerned regarding Genentech’s change to a specialty distributor system for bevacizumab, trastuzumab, and rituximab.

We are especially concerned because of the vital role that these three agents play in the treatment of patients with cancer, and the significant barriers and burdens that the new policy produces to providing optimal oncology care.

We appreciate Genentech’s stated goal of improving patient safety, integrity of the medicines, and ensuring access. The NCCN shares this philosophy and these goals and believe that the wholesaler model serves these goals exceptionally well. However,

NCCN is concerned that this change will have a strongly negative impact on business processes, facility demands, patient access, and financial demands on patients.

The logistics of drug procurement using a specialty distributor-only model as opposed to wholesalers increase the probability of inadequate or untimely supply of medication at the point of care and the time of need. This will force the stocking of higher inventories and serve to drive up costs of inventory and ultimately higher costs to our patients.

NCCN pharmacists note that the entire specialty distributor model is substantially inferior (operationally, ecologically, and financially) to the wholesaler model from the standpoint of the cancer care provider. Every aspect of the specialty distributor model creates operational hurdles necessitating significantly more time, effort and expense to achieve the same goal.

Our members have voiced that the financial impact resulting from this change will have a deleterious effect. The loss of wholesaler rebates will transfer a significant financial burden directly to care providers, which ultimately will be passed on to patients.

On behalf of our 25 leading cancer centers, NCCN urges you to reconsider this unfortunate decision. Please continue to distribute bevacizumab, trastuzumab, and rituximab through the traditional distribution channels.

NCCN has always worked collaboratively with Genentech, and we value our relationship. Through our collaborations, we are pleased to have had a positive impact on the delivery of high quality oncology care in this country. On behalf of our Member Institutions, we would like to work together to find a resolution to this situation.

Please do not hesitate to contact me directly should you have any clarifying questions or comments. At your request, NCCN would welcome the opportunity to meet with Genentech colleagues to discuss the changes to the distribution system.

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## ASCO Endorses Joint Guideline For Molecular Testing

The American Society of Clinical Oncology endorsed a joint clinical practice guideline on molecular testing published by the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology.

The guideline focuses on the selection of patients with lung cancer for therapies targeting epidermal growth factor receptor and anaplastic lymphoma kinase, and defines which patients should be offered EGFR and ALK genetic testing, and when and how such testing should be performed.

“This guideline is incredibly important, as it increases the ability to personalize lung cancer care and improve outcomes for patients with advanced lung cancer,” said Natasha Leighl, co-chair of the ASCO expert panel that endorsed the guideline.

“It describes the current evidence and helps oncologists and pathologists understand and put molecular testing into clinical practice,” Leighl said. The endorsement was published in the *Journal of Clinical Oncology*.

[The guideline](#) comprises 37 recommendations, consensus opinions, or suggestions. Key recommendations include: offering EGFR and ALK testing to all patients with lung adenocarcinoma irrespective of characteristics such as gender, race and smoking status; the use of a range of testing methods, provided they meet certain technical requirements, with certain types of tests not recommended;

adherence to guidance regarding specimen processing, testing validation, quality assurance, and turnaround times for reporting results.

CAP, IASLC and AMP are currently updating their guideline based on new evidence regarding ALK testing, testing for molecular alterations associated with acquired resistance to EGFR and ALK inhibitors, new markers such as ROS1, RET, ERBB2 (HER2), BRAF, MET and next-generation sequence testing.

## IARC Publishes Fourth Edition Of European Code Against Cancer

The fourth edition of the European Code Against Cancer was published by the International Agency for Research on Cancer, with the participation of the European Commission.

The code lists 12 ways to adopt healthier lifestyles and boost cancer prevention across Europe based on available scientific evidence. It is the outcome of a two-year collaborative work between cancer specialists, scientists, and other experts from across the European Union.

“The code raises awareness of the critical role of prevention in the fight against cancer,” said Christopher Wild, director of IARC, the specialized cancer agency of the World Health Organization. “By adopting the code, all European citizens can take concrete actions for themselves, their friends and families to significantly reduce their risk of developing cancer.”

[The code](#) emphasizes the importance of avoiding tobacco, alcohol, and excessive sun exposure as well

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as the benefits of maintaining a healthy body weight and being physically active. It also recommends participation in bowel, breast and cervical cancer screening programs.

Other recommendations include breastfeeding, vaccination against human papillomavirus, and limiting the use of hormone replacement therapy. It also recommends finding out about potential exposure to radiation from radon at home.

Since the publication of the previous edition of the code in 2003, 13 new member states have joined the European Union, and the code has integrated a greater diversity of people with a variety of lifestyles and associated cancer risk. The scientific justifications for the code will also be published in a scientific journal and will be made available to the general public on the IARC website.

### *In Brief*

## **Giles Named Deputy Director Of Lurie Cancer Center**

**FRANCIS GILES** was named deputy director of the **Robert H. Lurie Comprehensive Cancer Center** of Northwestern University.

Giles will oversee Northwestern Medicine's clinical research cancer programs and developmental therapeutics initiatives.

Giles previously served as the Lurie Cancer Center's associate director for translational research and developmental therapeutics, and has been director of the Northwestern Medicine Developmental Therapeutics Institute since 2013. He is also a fellow of the Royal College of Physicians of Ireland, the Royal College of Pathologists, and the European Academy of Cancer Sciences.

"We have ambitious goals for the next few years, and our rapidly evolving translational programs will establish the Lurie Cancer Center as a national and international destination for tailored developmental therapeutics," Giles said.

**ZHU CHEN** was honored by the **American Association for Cancer Research** with its Award for Distinguished Public Service and Global Impact in Cancer Research in Biomedical Science.

Chen, a fellow of the AACR Academy, is the vice chairman of the 12th Standing Committee of the National People's Congress. From 2007 to 2013, he served as China's minister of health. He received the award Oct. 9, where he delivered the opening plenary lecture at the AACR's inaugural meeting in China.

Chen helped pioneer the concept of combination targeted therapies for cancer and, by combining traditional Chinese medicine with Western medicine, he provided the first successful model in the treatment of acute promyelocytic leukemia with all-trans retinoic acid and arsenic trioxide.

Under Chen's leadership, the Chinese National Human Genome Center has contributed to human genome sequencing and SNP HaploMap projects. They recently completed genome sequencing of *Schistosoma japonicum*, which revealed features of a host-parasite interplay that lead to better control and prevention of infection, a disease that remains a significant health problem in China.

**LILI YANG** received the \$2.3 million **Director's New Innovator Award from NIH** for research into developing ways to genetically program blood stem cells to attack cancers. Yang is an assistant professor of microbiology, immunology and molecular genetics at UCLA Jonsson Comprehensive Cancer Center.

Her research focused on T cells and a smaller group of invariant natural killer T cells, which have a remarkable capacity to mount immediate and powerful responses to disease when activated. She and her colleagues hope to develop therapies designed to increase the number of iNKT cells in the blood.

"The potential for iNKT T cell receptor-based gene therapy is very exciting because it is very different from conventional T cell receptor-based gene therapy, which can only target specific types of tumor and a certain group of patients," said Yang. "The kind of iNKT T cell receptor gene therapy we are investigating could have universal application, treating many types of cancer and a large group of patients no matter what types of tumor they have."

**THE INDIANA UNIVERSITY Melvin and Bren Simon Cancer Center** was recognized by NCI as a designated cancer center, and had their support grant increased by 20 percent, following an in-depth peer review.

NCI rated the cancer center's research activities as "excellent," and awarded it a five-year, \$7.8 million support grant. The NCI designation places the IU Simon Cancer Center in a group of 68 cancer centers. It is the only NCI-designated cancer center in Indiana that provides patient care. The center first received the NCI designation in 1999, seven years after its founding.

"We are especially honored to be renewed with this very prized designation again," said Patrick

Loehrer, director of the IU Simon Cancer Center. “To receive a funding increase in the current funding climate is icing on the cake.”

Reviewers, composed of NCI officials and others from NCI-designated cancer centers, evaluated the cancer center’s five research programs and visited in February 2014. Members of those research programs are on the Indiana University-Purdue University Indianapolis, IU Bloomington, IU South Bend and Notre Dame campuses.

**CANCER TREATMENT CENTERS OF AMERICA** launched a fertility preservation program, **OncoPrez**, at its hospitals in Chicago, Philadelphia and Tulsa.

The program makes discussions about fertility and family planning an integral part of treatment planning for all men and women of childbearing years. The program will be offered at CTCA hospitals in Atlanta and Phoenix in early 2015.

Each CTCA hospital in the program has identified a local, dedicated fertility center to provide preservation services. Patients who are interested in exploring fertility preservation are provided with a direct referral to a reproductive specialist who will work collaboratively with the patient’s CTCA oncology team.

**THE ROBERT H. LURIE COMPREHENSIVE CANCER CENTER** and the Northwestern Medicine Developmental Therapeutics Institute entered into an alliance with **Perthera Inc.** to conduct a translational research program designed to assess the utility of integration of next generation sequencing, proteomic, and phospho-proteomic data in oncology developmental therapeutics and clinical practice.

The Lurie Cancer Center and NMDTI will work with Perthera on clinical protocols that incorporate Perthera’s approaches and methodologies to cancer protocol treatment and will assess the impact on overall disease management and patient outcomes.

Separately, in June, Perthera announced a partnership with the Pancreatic Cancer Action Network to identify relevant pathways and mutations for pancreatic cancer, including previously unidentified targets.

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**THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY** published a revised template for **survivorship care plans**.

Plans should contain information about treatment the patient received, their need for future checkups and cancer tests, the potential long-term late effects of the treatment they received, and ideas for ways survivors can improve their health, according to ASCO.

The new template, updating a previous version the society developed nearly a decade ago, was published in the *Journal of Oncology Practice* as part of a statement on the importance of complete survivorship care plans. The template is also part of ASCO’s Cancer Survivorship Compendium, and is available through ASCO’s [patient information website](#).

### Drugs and Targets

## **FDA Approves Velcade In Mantle Cell Lymphoma**

**FDA approved bortezomib (Velcade) injection** for previously untreated patients with mantle cell lymphoma.

The approval is based on the results of an international, randomized, head-to-head phase III study that showed that previously untreated patients receiving a bortezomib-containing combination (bortezomib, rituximab [Rituxan], cyclophosphamide, doxorubicin, and prednisone) experienced a 59 percent relative improvement in the study’s primary endpoint of progression-free survival (HR=0.63; p < .001)

The open-label prospective study evaluated 487 patients with previously untreated mantle cell lymphoma who were ineligible or not considered for a bone marrow transplant.

Patients in the bortezomib arm had a median PFS of 25 months, compared to 14 months in patients who received the standard R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) at a median follow-up of 40 months. The complete response rate for patients receiving the bortezomib combination compared to R-CHOP was 44 vs. 34 percent.

Bortezomib was previously approved for the treatment of relapsed or refractory mantle cell lymphoma in 2006.

**FDA granted priority review status to lenvatinib mesylate** as a treatment for progressive radioactive iodine-refractory differentiated thyroid cancer.

Developed by Eisai Inc., lenvatinib is an oral

multiple receptor tyrosine kinase inhibitor that blocks the kinase activities of vascular endothelial growth factor receptors, in addition to other proangiogenic and oncogenic pathway-related tyrosine kinases thought to be involved in tumor proliferation. These include fibroblast growth factor receptors, the platelet-derived growth factor receptor PDGFR, KIT and RET, which are thought to be involved in tumor proliferation.

Lenvatinib was granted orphan drug designation in various types of thyroid cancer in the U.S., Japan, and Europe. It is currently under investigation in thyroid, hepatocellular, endometrial, non-small cell lung cancer, and other solid tumor types.

**FDA granted priority review** to the investigational bispecific T-cell engager antibody construct **blinatumomab** for the treatment of adults with Philadelphia-negative relapsed/refractory B-precursor acute lymphoblastic leukemia.

Amgen, the drug's sponsor, also submitted a marketing authorization application to the European Medicines Agency. The submissions include data from a phase II trial of adult patients with Ph-relapsed/refractory B-precursor ALL treated with blinatumomab, which met its primary endpoint.

Blinatumomab, the first of Amgen's investigational BiTE antibody constructs, has received orphan drug designation from the EMA and FDA, and breakthrough therapy and priority review designation from the FDA for the treatment of ALL.

Blinatumomab is designed to direct T cells against target cells expressing CD19, a protein found on the surface of B-cell derived leukemias and lymphomas. Blinatumomab is also being investigated in pediatric relapsed/refractory ALL, relapsed/refractory Philadelphia positive B-precursor ALL, minimal residual disease positive B-precursor ALL, relapsed/refractory non-Hodgkin's lymphoma, including relapsed/refractory diffuse large B-cell lymphoma.

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## Funding Opportunity **Stand Up To Cancer Canada To Fund Two Dream Teams**

Stand Up To Cancer Canada will support two, four-year cancer research dream teams with nearly \$20 million USD raised by SU2C Canada collaborators and from the charity's September telecast. The dream teams will focus their research on translational research in breast cancer and cancer stem cells.

The \$22.6 million CAD was raised together with Canadian Breast Cancer Foundation with support from CIBC, Cancer Stem Cell Consortium, Genome Canada, Canadian Institutes of Health Research, and the Ontario Institute for Cancer Research.

The American Association for Cancer Research International – Canada, SU2C Canada's scientific partner, issued calls for ideas.

Research proposals will be reviewed by the SU2C Canada Scientific Advisory Committee, co-chaired by Nobel Laureate Phillip Sharp, institute professor at the Massachusetts Institute of Technology and David H. Koch Institute for Integrative Cancer Research at MIT; and Alan Bernstein, president and CEO of the Canadian Institute for Advanced Research.

The Stand Up To Cancer Canada-Canadian Breast Cancer Foundation Breast Cancer Dream Team will provide up to \$6 million CAD. Ideas are invited for a translational cancer research project that will include new therapeutic interventions for breast cancer that would be expected to reduce progression and improve overall survival.

The Stand Up To Cancer Canada Cancer Stem Cell Dream Team will provide approximately \$10.6 million CAD, supporting a pan-Canadian team of researchers, clinicians and nongovernmental organizations focusing on the role of cancer stem cells and stem cell programs on resistance and treatment failure in cancer, with an emphasis on genomics.

Additionally, the two teams may each receive supplementary funds up to \$3 million over four years from OICR, to support clinical trial activities in the province of Ontario.

Letters of Intent must be submitted by Dec. 8 using [the proposalCENTRAL website](#). General information on eligibility criteria, the application process, and other details are available at [www.aacrCanada.ca](http://www.aacrCanada.ca). Inquiries may be directed to the AACR International-Canada at 416-797-5366 or [su2ccanada@aacrcanada.ca](mailto:su2ccanada@aacrcanada.ca).