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# OREGON FLIRTS WITH— AND QUICKLY ABANDONS—PLAN TO DENY MEDICAID PAYMENT FOR NEXT-GENERATION SEQUENCING

By Matthew Bin Han Ong

The Oregon Health Authority did a considerable amount of work to prepare a plan that would deny Medicaid coverage for next-generation sequencing tests in the state.

A review of medical literature it conducted resolved that “direct evidence of clinical utility is not available” for NGS. Then, a guidance was drafted, approved unanimously by an advisory panel, and brought forth to a public hearing Sept. 27.

But there, the proposal encountered stiff opposition from Oregonians, who argued that it would create a massive health disparity in the state. The younger Oregonians eligible for Medicaid would be denied access to precision oncology, while the elderly would continue to get access under Medicare.

“I want to thank everyone who spoke up to make sure that NGS for patients with cancer is covered by Oregon Medicaid,” Brian Druker, director of the Knight Cancer Institute at the Oregon Health & Science University, said to The Cancer Letter. “Your voices were clearly heard and I applaud the committee for ensuring that our most vul-

nerable patients have access to this cutting edge technology.”

Druker’s institution lobbied heavily to stop the plan. Meanwhile, the chair of the subcommittee that unanimously approved the draft guidance, Vinay Prasad, reports to Druker. In recent months, Prasad, a hematologist-oncologist at OHSU, has emerged as a leading critic of precision oncology.

Insiders say that a [Sept. 26 story](#) published in The Cancer Letter was circulated among those alarmed by the Oregon proposal, including those present at the Sept. 27 public hearing.

At the conclusion of the meeting, the Health Technology Assessment Subcommittee, a part of the OHA’s Health Evidence Review Commission, decided to table the draft guidance indefinitely.

According to those present, Prasad pushed for a motion to vote on the

draft guidance, despite opposition from attendees who testified at the meeting. The other subcommittee members refused to vote, and finally the motion to table the draft guidance passed unanimously. A randomized controlled trial would be needed to demonstrate clinical utility of NGS tests, Prasad said at the meeting. (Experts say such trials would be neither feasible nor ethical.)

## First-of-its-kind anti-NGS policy

Had it been enacted, the plan would have created an inferior standard of care for the poor in Oregon, depriving these patients of access to targeted therapies, mainstream oncologists and experts on disparities in cancer care said to The Cancer Letter.

Being the first-of-its-kind formal policy proposal by a government entity for denying coverage, the rationale for this recommendation could potentially have been used by other state Medicaid programs as well as by private insurers dredging for reasons to deny payment for NGS tests and treatments they may point to.

The draft guidance in question was previously approved by Prasad's subcommittee. Of the five members on the subcommittee, Prasad appears to be the only oncologist.

Druker said OHSU will do everything it can to prevent the draft guidance from becoming policy.

"At the Knight Cancer Institute, we are committed to doing everything we can to ensure that patients have access to life-saving diagnostics and therapeutics," Druker said to The Cancer Letter before the public hearing. "NGS testing is increasingly allowing us to individualize therapy, and it is vitally important that our policymakers understand that the opportunities NGS offers today are considerably more advanced than they were even two to three years ago.

"The most recent evidence strongly supports the clinical utility of NGS. We are well positioned to inform policymakers about these advances, so that Oregonians have access to this cutting edge technology."

Earlier this year, the Centers for Medicare & Medicaid Services issued a [National Coverage Determination](#) for diagnostic laboratory tests using NGS for patients with advanced cancer. This means that patients eligible for Medicare will be able to receive NGS tests. Foundation Medicine's FoundationOne CDx receives full coverage under the NCD, and several other tests receive coverage from some local Medicare contractors (The Cancer Letter, [March 23](#)).

The clinical utility of NGS testing and its role in precision oncology was the subject of debates at the 2018 annual meetings of the American Association for Cancer Research and the American Society of Clinical Oncology.

At both debates, Prasad, the chair of the Oregon subcommittee, took the con side, arguing against NGS testing and precision oncology (The Cancer Letter, [June 22](#), [Sept. 7](#)).

"I believe that in oncology, we cannot practice improvisational oncology. We cannot just merely have hunches, and let the average community doctor just prescribe drugs based on a Foundation Medicine report," Prasad said at the AACR [debate](#). "And yet, that's precisely what is happening in this country day in and day out, we have rampant off-label studies being performed.

"My conclusions: The rhetoric has outpaced reality; there are true successes here, but few," Prasad said. "Sequencing and drug should be paid for with research or commercial funds until proof of benefit. CMS, unfortunately, is not a research funder, they cannot be used that way. They have fiscal difficulties themselves, and they have to pay for services that have proven benefit.

"Is genome-informed cancer medicine generating patient benefit or just hype? I conclude that there is some benefit, but it is mostly hype."

The draft guidance prepared for the Sept. 27 meeting of the Health Technology Assessment Subcommittee concludes: "Next generation sequencing tests of solid tumor tissue are not recommended for coverage (strong recommendation)."

The document is posted [here](#).

The recommendation was unanimously approved for public comment by Prasad and three other subcommittee members on June 28, minutes show.

Adam Obley, an assistant professor of medicine in the OHSU Division of General Internal Medicine, conducted the review of evidence for the Medicaid draft guidance.

““

Your voices were clearly heard and I applaud the committee for ensuring that our most vulnerable patients have access to this cutting edge technology.

””

– Brian Druker

As chair of the subcommittee, Prasad was not "actively involved in the development of an initial draft coverage guidance before it is presented to the subcommittee," OHA officials said in a statement Sept. 26 to The Cancer Letter. "An OHA contractor (Center for Evidence-based Policy) writes the draft evidence summary portion of the draft coverage guidance. OHA/HERC staff write the draft coverage guidance recommendation based on the evidence summary. An initial draft of the coverage guidance goes to the subcommittee and is posted online in preparation for the public meeting.

"The chair has no role in writing the initial draft," OHA officials said. "They see a copy of the draft recommendation during a leadership call to prepare for the first meeting where it will be discussed. No changes typically result from the leadership call. At the HTAS meetings, subcommittee members re-

view the draft guidance, review public comment, and then deliberate about the recommendations. Changes to the draft guidance are made during these public subcommittee meetings.”

## Jumping from academic debate to coverage

While the ASCO and AACR debates were academic, the Oregon proposal amounted to an attempt to translate arguments previously voiced by Prasad into policy, critics say. Prasad did not respond to an email from The Cancer Letter.

In the draft guidance, the subcommittee said that there is no direct evidence of clinical utility of NGS tests:

“Published evidence is insufficient at present to establish the balance of benefits and harms associated with next generation sequencing,” the subcommittee wrote. “The potential benefit of broad companion diagnostic testing has not been established by clinical utility studies. There is also potential harm related to the use of next generation sequencing in promoting the use of more costly targeted therapies when equally effective (or more effective) conventional chemotherapy might be available.

“The impact of next generation sequencing on clinical outcomes (cancer-related morbidity and mortality) or clinical decision making has not been established. A single randomized controlled trial showed that molecularly targeted therapies perform no better than treatments selected at the clinician’s discretion for previously treated patients with metastatic solid tumors. Resource allocation would be significant for next generation sequencing and the associated targeted chemotherapy agents.

“Although personalized (precision) cancer therapy is of significant inter-

est currently, our recommendation for non-coverage of next generation sequencing tests is strong because there is no direct evidence of benefit, and the best available evidence does not yet establish survival advantage with targeted cancer therapies.”

## Creating a disparity

Had the Oregon Health Authority approved the subcommittee’s recommendation, Medicaid beneficiaries in the state will be placed at a greater disadvantage vis-à-vis wealthier Oregonians, said John Stewart, associate director of clinical research at the University of Illinois Cancer Center, University of Illinois at Chicago.

“The unwillingness to provide patients with targeted therapies based upon their genetic profile, I think, is unconscionable,” Stewart said to The Cancer Letter. “It would create a therapeutic divide between patients with high socioeconomic status and patients with lower socioeconomic status.

“[The draft guidance] does not make sense. The logic to me behind that is, ‘It’s okay to be elderly and sick, but it’s not okay to be poor and sick.’ That’s how the draft guidance reads to me, because you won’t have access to state-of-the-art diagnostics. This is potentially an assault on the treatment of underrepresented populations for cancer.”

A conversation with Stewart, who reviewed the draft guidance for The Cancer Letter, appears on [page 10](#).

Prasad should have recused himself from deliberations on policy recommendations against coverage for NGS tests, said Richard Goldberg, director of the West Virginia University Cancer Institute and the Mary Babb Randolph Cancer Center.

“I would say that he is not an unbiased evaluator of this technology,” Goldberg said to The Cancer Letter. “I would’ve said, ‘He should have.’ Because, if nothing else, it’s raising the question of: Is he grandstanding? Or is he being an unbiased judge?”

“If I were in his situation, I would’ve recused myself.”

Goldberg, who reviewed the draft guidance for The Cancer Letter, said the proposal would widen disparities in cancer treatment.

“My opinion is that patients should have equal access to technology that is becoming useful in improving outcomes, regardless of which insurer they are covered by,” Goldberg said. “There shouldn’t be disparities between private-paying insurers and government-paying insurers, and government insurers like Medicare vs. those that cover low-income individuals.

“I can tell you that every week, we’re doing NGS tests on Medicaid patients in West Virginia as well as on patients with every other kind of insurance.”

A conversation with Goldberg appears on [page 14](#).

## Are RCTs feasible? Ethical?

In a debate with Prasad at AACR’s annual meeting earlier this year, David Hyman, chief of the Early Drug Development Service at Memorial Sloan Kettering Cancer Center, said:

“What I did just for my own edification and knowledge, I went through the past seven FDA-approved—and this is inclusive of both regular approval and accelerated approval—indications based on a biomarker-selected population where the evidence was generated using single-arm, non-randomized, non-blinded data,” Hyman said at the time. “What you could see quite clearly

## Are Randomized Controlled Trials Necessary?

Efficacy data from non-randomized studies leading to FDA approval\*

Biomarker	Tumor Type	Drug(s)	N	ORR	PFS (months)
BRAF V600	NSCLC (>1 line)	Dabrafenib + Trametinib	57	63%	9.7
ALK fusions	NSCLC (prior criz)	Brigatinib	110 <sup>1</sup>	54%	11.1
ALK fusions	NSCLC (prior criz)	Alectinib	225 (2 studies)	46 - 48%	8.1 - 8.9
EGFR T790M	NSCLC (prior TKI)	Osimertinib	127 (T790M+)	61%	9.6
BRCA1/2	Ovarian (>2 priors)	Rucaparib	106 (2 studies)	54%	12.8 <sup>2</sup>
MSI-H/MMR-D	Solid Tumor	Pembrolizumab	149 (5 studies)	40%	Not Reached
BRAF V600	Erdheim Chester	Vemurafenib	22	63%	Not Reached

\*- Accelerated and regular. 1- at indicated dose, 2- ARIEL2 results only



Memorial Sloan Kettering Cancer Center #PrecisionDecision

is an overall response rate hovering in the 50+ percent range, with a median progression-free survival typically exceeding 9 months.

“When I look at this, I actually feel quite comfortable with prescribing based on this level of evidence,” Hyman said. “I might actually go one step further and say that it would be potentially unethical to randomize patients after evidence like this was generated.”

The AACR session is posted [here](#).

The Oregon draft guidance was excessively restrictive to patient access and innovation in precision medicine, said Jeff Allen, president and CEO of Friends of Cancer Research.

“The analysis conducted mistakenly conflates evidence regarding clinical utility of a NGS test with effectiveness of a targeted therapy and fails to fully understand the value of NGS diagnostics in patient care,” Allen said a com-

ment submitted to the subcommittee. “We urge HERC to revise its recommendation of non-coverage for NGS diagnostic tests to support use of this tremendous technology and promote innovation for improved patient care.”

Jeremy Warner, associate professor of medicine and biomedical informatics at Vanderbilt University, said that oncologists get NGS tests for patients with advanced solid malignancies to:

1. Determine prognosis,
2. Determine one or more treatments that might slow down the cancer,
3. Determine that certain treatments will not help slow down the cancer, and
4. Look for inherited (germline) variants that might have implications for unaffected relatives, in the future.

Warner, the ASCO 2018 Annual Meeting Education Committee track leader of the Health Services Research, Clinical Informatics, and Quality of Care track, debated Prasad at the ASCO annual meeting earlier this year.

“Regarding #1, it isn’t necessary because prognosis is already very poor in this setting,” Warner said to The Cancer Letter. “Regarding #4, most commercial NGS tests actually scrub these results out, so unless the test is specific for germline, it isn’t going to report heritable implications. However, it is quite possible that today’s variant of unknown significance (which is reported) might be tomorrow’s inherited mutation; see [link](#).”

“So that leaves #2 and #3. For #2, it is certainly the case that there are no FDA-approved tumor-agnostic targeted therapies; the one FDA-approved immunotherapy, pembrolizumab, has a trigger based on MSI status, which would probably (but not definitely) be

known without having an NGS test. Otherwise, all of the current evidence from basket trials is non-randomized and to my knowledge none of the drugs tested to date are recommended in a tumor-agnostic manner by compendia or guidelines.

“However, we are all awaiting the likely approval of larotrectinib for TRK fusions (regardless of cancer type) and the results announced at ASCO for LOXO-292 for RET fusions are promising as well. If and when these drugs are approved, it makes a strong case for NGS testing as there is only so much tissue and ‘one-off’ testing is going to exhaust the biopsy quickly.

“For #3, it gets complicated. For some, knowing that they had all the most modern testing and there are ‘no available treatments’ left can be closure of sorts (there is always best supportive care and palliative care, let’s not forget). For others, this could be seen as ‘taking away hope’ and could be psychologically damaging.

“Bottom line: For these sorts of complex tests with a panoply of possible results, a thorough discussion with the patient prior to ordering the test is paramount. And, of course, making sure to close the loop with a follow-up with face-to-face discussions. Unfortunately, in our fee-for-service driven practices, neither of these happens quite as often as it should.”

As written, the Oregon HERC is directing these patients only to toxic chemotherapy, said Vincent Miller, chief medical officer of Foundation Medicine.

“What’s at issue is that all patients diagnosed with cancer—regardless of economic status—have access to these tests, so that the full expanse of systemic treatment options, including FDA-approved targeted agents and mechanism-based clinical trials, can be identified for potential use,” Miller said to The Cancer Letter.

NGS tests can help physicians identify patients who may benefit from treatment with targeted therapies for a variety of cancer types, FDA said in a statement to The Cancer Letter.

“When FDA reviews these tests to determine their safety and effectiveness, we are assessing their analytical and clinical validity,” FDA officials said. “FDA does not require that test developers provide clinical utility as part of our review. However, some submissions may contain this.

“For example, sponsors often leverage therapeutic product clinical studies to support clearance or approval of companion diagnostics. Such trials may demonstrate clinical utility when the use of the test identifies which patients may benefit from a particular therapeutic.”

## The NCD fine points

CMS March 16 published the final NCD that pays for NGS in a broad range of cancers (The Cancer Letter, [March 23](#), [Feb. 3](#)).

The decision document is posted [here](#). To qualify for coverage under the NCD, laboratories must meet three conditions:

- FDA approval or clearance as a companion in vitro diagnostic;
- An FDA approved or cleared indication for use in that patient’s cancer; and
- Results provided to the treating physician for management of the patient using a report template to specify treatment options.

Labs that don’t have FDA approval or clearance may seek coverage from Medicare Administrative Contractors. MACs are usually reticent to provide such coverage.

Foundation Medicine clearly has benefited the most from the NCD.

Last November, the company’s FoundationOne CDx test received an FDA approval, and—concurrently—CMS issued a provisional NCD defining the settings where Medicare would cover the test (The Cancer Letter, [Dec. 1, 2017](#)). It was FMI that requested the NCD.

It’s left up to MACs to decide whether NGS tests provided by cancer centers, such as MSK-IMPACT, should be covered.

The NCD covers Stage III and IV, metastatic, recurrent, relapsed, or refractory cancers. The NCD provides coverage across all solid tumors.

Repeat testing is covered using the same diagnostic laboratory test using NGS in the same patient only when a new primary diagnosis of cancer is made.

The first joint CMS-FDA approval was given to Cologuard, a stool DNA test sponsored by Exact Sciences Corp. (The Cancer Letter, [March 28, 2014](#)).

There are two other NGS tests approved by FDA:

- The OncoPrint test, sponsored by Thermo Fisher Scientific, for targeted therapies for non-small cell lung cancer, and
- [Praxis Extended RAS Panel](#), used to detect genetic mutations in RAS genes in tumor samples of patients with metastatic colorectal cancer. The test is sponsored by Illumina Inc.

Both tests are approved for specific genes and tumor types. Neither OncoPrint nor Praxis has gone through parallel review by CMS.

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*Paul Goldberg contributed to this story.*



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The Cancer Letter.

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CONVERSATION WITH  
THE CANCER LETTER

## UIC's Stewart: Oregon draft guidance is "an assault on the treatment of underrepresented populations"

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It does not make sense. The logic to me behind that is, "It's okay to be elderly and sick, but it's not okay to be poor and sick." That's how the draft guidance reads to me, because you won't have access to state-of-the-art diagnostics.

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**John Stewart**

*Associate director for clinical research, University of Illinois Cancer Center, University of Illinois at Chicago*

**Matthew Ong:** What do you think of the draft guidance by the subcommittee? What are your general impressions?

**John Stewart:** It was striking. I looked at things through a holistic value-based care model where we provide the right care to the right patient at the right time.

So, absent having next-generation sequencing, we're basically giving un-directed chemotherapy, or limited chemotherapy.

In other words, we would recognize that a patient had, for instance, an ER/PR+ tumor and that will result in one therapeutic approach. If that approach fails, we move to second-line therapy—again, that is kind of an empiric therapy.

Now, what next-generation sequencing does is it allows us to understand specific drug targets that might work and will allow us to get to that appropriate next line of therapy that is tailored for that patient.

And so, what this ruling would do is that it potentially prevents us from providing tailored therapy to patients.

**Specifically patients in Oregon who rely on Medicaid.**

**JS:** Exactly.

**Their recommendation is for non-coverage of NGS tests for solid tumor tissues, because they say that there is no direct evidence of clinical utility for patients with advanced solid malignancies. Is this true?**

**JS:** The emergence of personalized medicine speaks to the necessity of there being next-generation sequencing for patients that move beyond first-line therapy.

I will tell you that this is particularly interesting to me, not just from a value-based care model, but also, this would create a system where a group of individuals, based upon their socioeconomic status, do not have access to state-of-the-art care.

So, what we're doing is we're creating a treatment divide that, again, is based upon socioeconomic status. Now, I think that there is a moral imperative for us to better understand their reasoning behind this ruling.

I could not see specifically who was on that advisory board.

**Vinay Prasad is the chair.**

**JS:** Who? Vinay Prasad? I don't know him. Is he an oncologist?

**He's a hematologist-oncologist at the Oregon Health & Science University. He debated proponents of precision oncology this year at both ASCO and AACR, saying that genome-informed cancer medicine is "mostly hype."**

**JS:** So, he clearly had a pre-formed opinion about this?

**I'd say so. He made it quite clear in his presentations, saying that there's some benefit, but it's mostly hype.**

**JS:** He had a pre-formed opinion, so he probably should've recused himself from the conversation.

**Since the subcommittee concluded that there is insufficient evidence, do they think that CMS made an error when it issued the National Coverage Determination for NGS tests? From what you know, is there evidence of clinical utility?**

**JS:** In terms of citing specific data points, I don't have that in front of me, if you gave me a day or two, I could pull it up. But, like I said, the fact of the matter is that we have the ability to understand what the appropriate treatment regimens are for patients based upon genomic data.

The unwillingness to provide patients with targeted therapies based upon their genetic profile, I think, is unconscionable.

If you read through that draft guidance, what it basically said is, “Yeah, you know, many of the people who have stage III and stage IV disease are ultimately going to become disabled, and then they will go to Medicare. Let Medicare pay for it.”

Yes, that’s what some of the [sub-committee] discussion [in the meeting’s minutes] essentially said.

**Why would policymakers push patients toward Medicare, when you can pay for them now?**

**JS:** Yes, and so again, it really gets to the value in medicine question of providing the right care to the right patient—at the right time. It’s not cost shifting, right?

Because what they’re looking to do is to cost-shift to Medicare.

**How is that the right thing to do? How would treatment be effective if you wait for patients with metastatic disease to become disabled?**

**JS:** That’s a zero-sum game, there. It is unfortunate.

**How does it make sense for patients over 65 to get coverage for NGS tests, but not for low-income patients via Medicaid?**

**JS:** It does not make sense. The logic to me behind that is, “It’s okay to be elderly and sick, but it’s not okay to be poor and sick.” That’s how the draft guidance reads to me, because you won’t have access to state-of-the-art diagnostics.

**Would this exacerbate disparities?**

**JS:** Yes, it would. It would create a therapeutic divide between patients with high socioeconomic status and patients with lower socioeconomic status.

**If this becomes real policy at some point in Oregon, does it set a precedent for Medicaid programs in other states? Do you know of any other state Medicaid program that is trying to do this?**

**JS:** It does. I don’t know if others have done it, but the precedence will surely follow. So, if we think about states that did not expand Medicaid, then they are at real risk, because they will tend to have straps on Medicaid budgets.

**And they will try to cut any coverage if they can find a rationale for doing so?**

**JS:** Yes.

**What about private insurance companies? Will they also use this as an example and say, “Well, why should we pay if Oregon doesn’t?”**

**JS:** Most private insurance companies kind of base their decisions on CMS decisions. I don’t think that it will have a sustainable impact on private insurers. If private insurance companies try to challenge this, then there’s a CMS coverage that will be able to provide a fallback. Very rarely do state Medicaid decisions provide coverage fallback for private insurance.

**If this does happen in Oregon, does it have any implications for research in precision oncology in the state?**

**JS:** The proposed policy concerns me at a state Medicaid level, both locally and potentially nationally. This is potentially an assault on the treatment of underrepresented populations with cancer.

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CONVERSATION WITH  
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## WVU's Goldberg: Oregon draft guidance would widen disparities for low-income cancer patients

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**Richard Goldberg**

*Director, West Virginia University Cancer Institute  
and the Mary Babb Randolph Cancer Center*

**Matthew Ong:** What were your first thoughts when you read the [draft guidance by the subcommittee](#)?

**Richard Goldberg:** My first thoughts are that it has become a standard part of practice to do NGS on patients. I work in the GI oncology world, and mainly do colon cancer, and we do it on patients at first sign of metastasis, partly because we need RAS testing, but also because we're looking for tumors that exhibit microsatellite instability, as those tumors are more likely to respond to treatment with immuno-oncology agents.

The main reasons for wanting to do NGS is that if you can find a driver mutation with a specific drug that's targeted to it, or if you can find that tumors have a high mutational burden and are more likely to respond to an immuno-oncology agent, you can give patient those options. So, I would say that most sophisticated patients and most sophisticated oncologists are doing this testing.

Every week, I have another vendor coming in—you've got Caris, Foundation Medicine, Orion, groups that are doing the blood-based assays—there's huge investment in this technology and a huge marketing effort for it. The utility of NGS is becoming more apparent every year, and the field is changing rapidly so that, looking at the outcomes of analyses that were done in 2015 as was done by the Oregon tribunal, those are recording data that were done before then, at a time when we understood the technology less well, and a time when we had fewer targeted options.

At one point in my life, I ran a new technology assessment committee for Geisinger Health Plan, which is an insurance company, and we had a panel

of people who deliberated and tried to decide when something had sufficient evidence to be covered. I'll give you an example—proton beam therapy for people with prostate cancer, which we wrestled with way back then.

This is sort of a similar circumstance; technology that's emerging. It is a difficult judgment to determine when it becomes standard or when is it experimental.

Clearly, it was standard enough that the FDA approved of NGS testing from Sloan Kettering and Foundation Medicine technologies and those two panels of genes. NCCN is recommending it, and Medicare is covering it. Those are all significant endorsements of the technology.

Since you say this is the standard of care in colon cancer—solid malignancies—and you use NGS testing routinely for your patients, why would the Oregon subcommittee say that there is no direct evidence of clinical utility in solid tumors?

**RG:** They cited, as you saw, several studies, all three of them from 2015—two of which show no survival benefit, one of which show there's survival benefit—and they used that as their database, I think.

Is that database cherry-picked?

**RG:** I think it is, likely. I have to admit that I haven't looked at all the data recently, but based on what I know, we are doing this standardly in lung cancer patients, in GI cancer patients, in melanoma patients. It's a standard of care in

the management of patients with advanced disease, particularly as they become refractory to standard therapies.

From your perspective as a director of a cancer center in West Virginia, if this recommendation is enacted in Oregon, what does this mean for low socioeconomic status patients who rely on Medicaid for cancer treatment? Would it harm them? Would this widen disparities?

**RG:** I do think it will have the potential to widen disparities, because patients with private insurance will often get coverage for this, and therefore, will have more options than those who don't get this testing done, because they lack insurance coverage of NGS testing. It's gotten to the point where, for studies like ASCO's TAPUR, having genotyping done is necessary to be considered for the trial. And so, both on and off trials, this is relevant.

Is it bad science to deny access to NGS testing?

**RG:** My opinion is that patients should have equal access to technology that is becoming useful in improving outcomes, regardless of which insurer they are covered by. There shouldn't be disparities between private-paying insurers and government-paying insurers, and government insurers like Medicare vs. those that cover low-income individuals.

I can tell you that every week, we're doing NGS tests on Medicaid patients in West Virginia as well as on patients with every other kind of insurance.

Has West Virginia's Medicaid program made a coverage determination for NGS tests?

**RG:** Not that I'm aware of.

If this becomes real policy in Oregon, does it set a precedent for Medicaid programs in other states, including West Virginia, for instance?

**RG:** I would think it does, because there is no obligation for a state to follow a national coverage determination, as I understand it. That is because Medicaid is a state-administered and funded program.

Would private insurers also look at something like this and say, "Look, Oregon isn't paying for it, so that's our scientific rationale"?

**RG:** Yes, I think that's also a possible outcome of this. In the end, these deliberative bodies are made up of people who are educated, but variably expert on the technologies that they are evaluating, in a time when the utility of technologies is evolving extremely quickly.

So, I think it's reasonable to ask the question, "Did they evaluate the most up-to-date data that's out there in making their decision, and how different is the data going to be after this year's ASCO than it was after last year's ASCO?"

In another interview, someone asked me who Vinay Prasad is and I said he was known this year for the debates at ASCO and AACR...

**RG:** ...who gave the various "no utility to personalized medicine" talks? Yes. I would say that he is not an unbiased evaluator of this technology.

Another oncologist, who is quoted in this story, also said that since Prasad had "preformed opinions," Prasad should've recused himself from the conversation. I don't know if this is the right question to ask, but since he's not unbiased and believes that precision oncology is "mostly hype," do you think it's ethical for him to chair this subcommittee?

**RG:** I think it's ethical for him to chair this subcommittee. Whether he should've recused himself from this particular deliberation is another question, and I would've said, "He should have."

Because, if nothing else, it's raising the question of: Is he grandstanding? Or is he being an unbiased judge?

If I were in his situation, I would've recused myself.

From this particular deliberation that has real impact on cancer treatment for Medicaid patients in his state.

**RG:** Right.

Did I miss anything?

**RG:** I would say that, based on my personal experience with findings from NGS, I have made therapeutic recommendations that have been of value to patients. The difficulty with that is individual patients vs. populations of patients, and the relative cost-effectiveness of doing the evaluations.

In my opinion, and that would be in my experience, it is cost-effective, while the Oregon subcommittee made a decision that it wasn't.

And I believe that there is room for disagreement in this setting, that a person who is a bit of a contrarian about this new technology should have recused himself from this conversation.

“

It's a standard of care in the management of patients with advanced disease, particularly as they become refractory to standard therapies.

”



# In Baselga's wake: Debate focuses on COIs of academics on boards of for-profit firms

By Paul Goldberg

As the fallout from the ethics scandal at Memorial Sloan Kettering Cancer Center continues, cancer center officials are investigating allegations contained in an anonymous letter from a group that identifies themselves as “Concerned Employees of MSKCC.”

Also, an ethics task force formed by MSK in the aftermath of the conflict of interest imbroglio will focus on the question of whether cancer center employees should be allowed to serve on the boards of directors of for-profit companies.

José Baselga, MSK's ousted chief medical officer and physician-in-chief, whose failure to disclose competing interests had triggered the crisis at the cancer center, served on the boards of Bristol-Myers Squibb Co. and Varian Medical Systems Inc. (The Cancer Letter, [Sept. 14](#)). He was forced off those boards after he submitted a resignation from his MSK positions (The Cancer Letter, [Sept. 21](#)).

Craig Thompson, MSK president and CEO, serves on the board of directors of Merck.

Here, the MSK recommendations of the MSK task force could have broad ramifications, as academics from many institutions serve on the boards of pharma and biotech companies.

Consider Merck's board. Besides MSK's Thompson, it includes the following academics:

- Thomas Cech, an investigator, Howard Hughes Medical Institute, Distinguished Professor at the University of Colorado, and director of the University of Colorado BioFrontiers Institute.
- John Noseworthy, president and chief executive officer at Mayo Clinic and professor of neurology, Mayo Clinic College of Medicine & Science.
- Paul Rothman, dean of medical faculty and vice president for medicine,

The Johns Hopkins University, and CEO, Johns Hopkins Medicine.

Members of the boards of directors represent the interests of the companies' shareholders. In some cases, these interests can clash with the interests of academic institutions where the board members in question hold their day jobs. Sometimes these conflicting interests can be easily managed; sometimes not.

The fallout from The New York Times and ProPublica [Sept. 8 story](#) about Baselga's years-long failure to disclose conflicts of interest continued, as the Times editorial board on Sept. 16 published an [editorial](#) about conflicts of interest at the cancer center.

Another Times-ProPublica [story](#) published on Sept. 20 questioned MSK's role in establishing [Paige.AI](#), an artifi-

“  
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 are very aware of the  
 disappointment and  
 distress that many of  
 you are experiencing  
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 at our Center.”

— DeAngelis and Thompson

cial intelligence start-up that aims to use the hospital’s pathology archive—consisting of tissue slides from 25 million patients—to develop deep learning algorithms and create a decision support system for pathologists.

Late last week, a group of MSK employees submitted an anonymous letter to the hospital’s administration. The letter demands a public airing of conflicts that involve Baselga and other MSK officials.

The Cancer Letter doesn’t publish anonymous material, particularly if the source and author’s identity is unknown to us.

In this case, the letter is summarized and partially quoted, because MSK’s officials acknowledged the letter and hired outside counsel to investigate the allegations it contains.

“In addition to an independent investigation into the aforementioned conflicts, we call on all officers and board members of MSK to immediately divest themselves of any equity stake in companies doing business with MSK-CC,” the letter states. “We further call on them to resign from any boards of companies that have contractual relationships with MSK.

“Going forward, no officer or board member should be allowed to serve on the board of or have an equity stake in any company financially involved with our center. Nothing short of the above will restore the public’s trust in our institution.”

The anonymous letter focuses on five areas of Baselga’s potential conflicts of interest:

- Was Baselga’s recused from business related to GRAIL, a liquid biopsy company where he serves on the scientific advisory board?
- Did Baselga play any role in managing an MSK phase I study of a prod-

uct of Infinity, a company where he was a director?

- What role did Baselga play in development of an MSK proton beam center in conjunction with Varian, a company that named him to the board in 2017?
- Did Baselga play a role in Varian’s decision to make an investment in GRAIL?
- How did MSK manage Baselga’s role in running the APHINITY trial for Roche/Genentech at the time of that company’s acquisition of Seragon Pharmaceuticals? Baselga was paid \$3 million by Roche for his equity stake in the start-up.

On Monday, Sept. 24, Thompson and Baselga’s interim replacement Lisa DeAngelis sent out the following memo to the medical staff:

Dear MSK Colleague,

We and our board are very aware of the disappointment and distress that many of you are experiencing after recent events at our Center. We share these concerns and are deeply sorry that you feel let down. As your leaders, we recognize that nothing is more important than maintaining the integrity and reputation of MSK and its staff.

We believe that it is imperative that faculty and staff are able to voice their views around these issues and other pressing institutional issues of concern. We want to let you know that in addition to the Task Force that was announced to review our conflict of interest (COI) policies and procedures, the elected leadership of the Medical Staff is creating a forum for faculty and staff to voice their concerns and ideas which we will communicate directly to the institutional Task Force.

There will be several ways for you to voice your views. Submit your feedback by email ([osquestions@msk-cc.org](mailto:osquestions@msk-cc.org)) or via SurveyMonkey ([here](#))

The Medical Staff leaders are also planning a town hall this Friday, September 28, at 8:00 am in the Zuckerman Auditorium. This follows the Wednesday meeting of the MSK Boards of Overseers and Managers. In parallel, the board will review MSK's processes and policies concerning COI.

One of the specific issues that we requested the COI Task Force to examine is whether any senior leader of MSK should be permitted to serve on the board or as a consultant of a for-profit corporation.

We also recognize that communications and transparency need improvement. That's a commitment we are making.

We have complete confidence in the outstanding care delivered every day to our patients and their families, and we know you do this with compassion and integrity. This is one of MSK's core missions. However, there is internal and external concern that this mission has been compromised. Nothing could be further from the truth because each of you guarantees that this mission is accomplished daily with every clinical encounter. Senior leadership is committed to working with you to ensure ethical and transparent principles and policies to achieve our goals of superb care, education and developing the therapies of tomorrow.

Medical Staff Leadership include:

- President – Nadeem Abu Rustum
- President-Elect – Diane Reidy

- Past President – Jedd Wolchok
- Alternate – Anne Covey
- Alternate – Richard Wong
- Chair, Junior Faculty Council – Lisa Ruppert

We look forward to hearing from you.

Regards,  
Lisa and Craig

The following day, Thompson and DeAngelis sent out a memo that acknowledged the existence of the anonymous letter. The concerns in the letter are "without merit," they wrote. The text of the email follows:

Dear MSK Colleagues,

In light of recent events, we have received emails expressing some concerns. We take all statements of concern seriously, whether by staff, by patients, or by external stakeholders. An internal review of the issues raised has already begun and we believe those concerns to be without merit. In addition, MSK's Chief Compliance Officer is engaging outside counsel to conduct a focused review.

As always, we encourage staff to refer concerns to the confidential compliance hotline at 866-546-5421. For more information about MSK's compliance program, the [Code of Conduct](#) is a helpful resource.

Regards,  
Lisa and Craig

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# Moving Breast Cancer Treatments Forward

October 17, 2018  
Bethesda, MD  
8:00am-4:30pm

Register at  
[www.jktgfoundation.org](http://www.jktgfoundation.org)



Register today for this free conference featuring more than a dozen leading breast cancer researchers. Helen Piwnicka-Worms, Ph.D., MD Anderson Cancer Center, will give the 3rd Annual Jayne Koskinas Memorial Lecture and the day's panel topics include:

- New leads from the clinic and other new developments
- What does Immuno-Oncology hold for breast cancer patients: can the limiting of toxicity issues be overcome?
- Converging common biology and treatment paradigms in breast and ovarian cancer
- Issues, problems and potentials in breast cancer brain metastasis
- Interdisciplinary collaborations: identifying solutions efficiently

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## IN BRIEF



## NIH receives \$2B raise as House passes FY19 spending package

The House of Representatives Sept. 26 passed the fiscal year 2019 “minibus” funding bill, increasing the NIH appropriation by \$2 billion to \$39.1 billion—a 5.4 percent boost over the current level.

Of the proposed \$2 billion, \$190 million in new money would trickle down to NCI. The combined Defense, Labor-HHS appropriations package brings NCI’s budget to a total of \$6.1 billion, including \$400 million in Moonshot funding (The Cancer Letter, [Sept. 21](#)).

President Donald Trump is expected to sign the bill before the end of the fiscal year.

With the completion of this package, Congress will have approved 75 percent of all annual discretionary funding prior to the end of the fiscal year on Sept.

30—a critical step in returning to the regular federal funding process, and an achievement that has not occurred in over two decades. This is also the first time in over 20 years that Congress has passed a Labor-HHS bill prior to the end of the fiscal year, and the first time in over 10 years it has passed a Department Of Defense bill prior to the end of the fiscal year.

“This package also includes a short-term continuing resolution to keep the federal government open and operational until all 12 Appropriations bills can be signed into law,” House Appropriations Chairman, Rep. Rodney Frelinghuysen (R-NJ), said in a statement. “This will avoid the threat of any government shutdown, and allow for time for work on the remaining funding bills to be completed.”

Passage of the measure before the end of the current fiscal year is noteworthy, and congressional leaders should be commended for their commitment to advancing the bill in a timely fashion, said Mary Woolley, president and CEO of Research!America.

“The \$2 billion increase for NIH builds on the momentum to accelerate research into precision medicine, Alzheimer’s disease, cancer, and other health threats,” Woolley said in a statement. “Funding for the Agency for Healthcare Research and Quality to support health services research is critical to addressing inefficiencies and waste in our health care system. The measure will also enable the Centers for Disease Control and Prevention to step up efforts to combat antibiotic resistance, and the opioid epidemic through research, treatment and prevention.”

## NIH memorial service for Alan Rabson scheduled for Oct. 30



A memorial service for Alan Rabson will take place on Oct. 30, from 2 to 4 p.m., at the Ruth L. Kirschstein Auditorium, Natcher Conference Center in Bethesda, MD.

Rabson, a premier cancer pathologist whose most recent title at NCI was scientist emeritus, died on July 4. He was 92 (The Cancer Letter, [July 6](#)).

A reception, hosted by the Foundation for the National Institutes of Health, will follow the service, “Alan S. Rabson, MD: Celebrating a Life in Science Leadership, and Patient Care.”

Register [here](#). To share memories or photos, visit the Sentiments page.

## Heidi Nelson named medical director of the American College of Surgeons Cancer Programs



Heidi Nelson, a colorectal surgeon from Mayo Clinic, was named medical director of Cancer Programs in the American College of Surgeons Division of Research and Optimal Patient Care.

Nelson succeeds David Winchester as he transitions from the position he has served in for more than 30 years. Nelson comes to the ACS from her position as chair, and vice chair for research, of the department of surgery, Mayo Clinic, as well as professor of surgery, Mayo Clinic College of Medicine and Sciences, Rochester, Minn. She has master's faculty privileges in clinical and translation science at the Mayo Clinic Graduate School of Biomedical Sciences and the Mayo Clinic College of Medicine and Science.

As the Fred C. Andersen Professor for the Mayo Foundation and a consultant for Mayo Clinic's division of colon and rectal surgery, Nelson is internationally renowned for her research in the field of colon and rectal cancer.

Nelson's work has also helped reduce the cancer burden in patients with locally advanced and recurrent rectal cancer through studies examining the role of complex surgeries and intraoperative radiation therapy. Nelson will be starting at the ACS later this month.

## American Cancer Society honors John Ruckdeschel with St. George Award



The American Cancer Society recognized John Ruckdeschel, director of the University of Mississippi Medical Center Cancer Institute and professor of medicine in the Division of Hematology and Oncology, for his work and his continuing support of the ACS.

ACS presented the St. George National Award to Ruckdeschel during a ceremony in Jackson on Sept. 20.

Ruckdeschel commended the ACS for its work on the Gertrude C. Ford Hope Lodge in Jackson, currently under construction adjacent to UMMC. The Hope Lodge is scheduled to open in early 2019 and will provide rooms for patients being treated at Jackson-area cancer centers and their family mem-

bers. Lodging and transportation to treatment are free.

Conceived in 1949 by Charles S. Cameron, former ACS medical and scientific director, the St. George National Award has been presented annually to ACS volunteers nationwide. Nominees must have served as leaders in the community, mission delivery and/or governance in more than one area of focus for a minimum of four continuous years and must represent ACS in a manner that advances the cause and expands community presence. The St. George National Award Task Force reviews all nominations and shares the award winners with the ACS Board of Directors.

Ruckdeschel is a medical oncologist with a focus on thoracic malignancies.

He is a former CEO at the Moffitt Cancer Center in Tampa, leading it to a NCI comprehensive designation. He later served as CEO of the Karmanos Cancer Institute in Detroit and the Nevada Cancer Institute in Las Vegas.

## Carlos Arteaga awarded \$600,000 to study breast cancer therapy resistance



The Susan G. Komen organization has awarded a \$600,000 research grant to Carlos Arteaga, director of the Harold C. Simmons Comprehensive Cancer Center and associate dean of oncology programs at UT Southwestern Medical Center.

The grant to Arteaga is part of a \$62 million investment by the Komen organization for research on drug resistance, triple negative breast cancer, and new treatments such as immunotherapies, as well as funding to reduce cancer health disparities.

Arteaga will study how estrogen receptor-positive breast cancers become hormone-independent and develop resistance to current anti-estrogen therapies. The research could lead to more precise treatment plans for breast cancer patients, potentially involving combinations of drug therapies to prevent the development of drug resistance.

## ASCO recognizes Rep. Kevin Yoder with 2018 Congressional Leadership Award



The American Society of Clinical Oncology has presented Rep. Kevin Yoder

(R-KS) with the 2018 Congressional Leadership Award.

Each year, ASCO presents this award to a member of Congress who has continuously supported legislation that promotes an improved practice environment for the oncology community and improves the quality of care for cancer patients.

A member of the House Appropriations Committee and Co-Chair of the House Cancer Caucus, Rep. Yoder has worked tirelessly over the last three years to build support for sustainable funding increases for NIH and NCI.

He signed the Dear Colleague Letter to HHS in October 2017, which called for a correction to the Merit-based Incentive Payment System score adjustment to ensure the score is not applied to Part B Drug payments. The issue was resolved in February 2018.

Rep. Yoder continues to demonstrate his support for individuals with cancer through co-sponsorship of the Childhood Cancer Survivorship, Treatment, Access and Research Act of 2017 (H.R. 820), the Palliative Care, Hospice, Education, and Training Act (H.R. 1676), the Cancer Drug Parity Act (H.R. 1409), and the Restoring Patient's Voice Act of 2017 (H.R. 2077).

## NCCN moves global headquarters to Plymouth Meeting

The National Comprehensive Cancer Network has moved into new headquarters in Plymouth Meeting, PA, near Philadelphia, from Fort Washington, PA. The new location will allow for greater hosting capacity for meetings, guests, and a growing staff.

## Cuomo announces U.S.-Cuba venture to develop new cancer treatments

New York Governor Andrew Cuomo announced Roswell Park Comprehensive Cancer Center has formed the Innovative Immunotherapy Alliance S.A., the first-ever biotech venture between the U.S. and Cuba.

The joint venture gives Roswell Park access to CIMAvax and three Cuban-developed cancer immunotherapy treatments not previously accessible to U.S. patients or researchers: IL-2 mutein, VSSP and another investigational immunotherapy that targets tumor-associated gangliosides.

While these agents are still investigational therapies in the U.S., evidence to date strongly suggests that all four are worthy of further study in several cancer types.

This joint venture biotech company, Innovative Immunotherapy Alliance S.A., will be based in Cuba and will be operated jointly by CIM's commercial affiliate, CIMAB S.A., and by a Roswell Park subsidiary, GBCT II LLC.

This initiative will move forward in accordance with permissions issued by the Office of Foreign Assets Control of the Department of Treasury, the Bureau of Industry and Security of the U.S. Department of Commerce and the U.S. FDA.

Roswell Park expects to initiate additional clinical trials, enrolling more than 100 patients in the U.S. within the next three years with plans for additional clinical studies to follow. Nearly \$4 million in donations is funding Roswell Park's initial CIMAvax clinical trials.

The Cuban phase II and phase III clinical trials of CIMAvax have shown increased overall survival and improvement in quality of life for patients with non-small cell lung cancer.

# THE CLINICAL CANCER LETTER



**Anne-Marie Langevin  
receives Harry Hynes  
Award**



Q

&

Langevin spoke with  
Paul Goldberg, editor and  
publisher of The Cancer Letter.

A



## CONVERSATION WITH THE CANCER LETTER

**A**nne-Marie Langevin, of the South Texas Pediatric Minority/Underserved NCI Community Oncology Research Program site in San Antonio, won the 2018 Harry Hynes Award, which is given annually to the PI who reflects the outstanding contribution to clinical trials and community research.

Langevin, professor of pediatrics and the Greehey Chair in Pediatric Oncology at UT Health San Antonio, is the PI at the only NCORP focused on pediatric underserved populations. The NCORP has enrolled over 2,000 children, adolescents and young adults on clinical trials. Altogether, 68 percent of the site's enrollment is minority, primarily Hispanics.

She has an interest in drug development and is a member of the Pediatric Oncology Experimental Therapeutics Investigators. During her leadership, Langevin created an NCI navigator program to provide access to Hispanic pediatric oncology patients near the borders of Texas and Mexico.

NCORP funding covers four independent pediatric programs. The award provides \$740,000 per year, plus intermittent supplements) for five years from 2014-2019.

The NCORP's Harry Hynes award recognizes local community researchers who embody the attributes of the leadership and commitment demonstrated by Harry Hynes, an Irish native who came to Wichita, Kan., in 1960 and went on to be a pioneer in developing one of the nation's first Clinical Community Oncology Programs in 1983.

Langevin spoke with Paul Goldberg, editor and publisher of The Cancer Letter.

**Paul Goldberg: Congratulations. It's great that you got the recognition.**

**Anne-Marie Langevin:** I was very surprised. I was, actually, shocked. I don't do what I do for recognition.

I do it because I like what I do. We all have good days and bad days, but as a whole it's all good.

Every so often I ask myself: Would I ever do anything differently, and the answer is always the same. No.

The day I stop loving it will be the day I will move out of the field.

**You are Canadian, I notice in your bio. Texas is far from Montreal.**

**AL:** I am Canadian. I was born and raised in Montreal, educated in French, then did my adult hematology, but then decided that I really liked pediatric oncology, and I applied to do full training at the Hospital for Sick Children in Toronto.

I did that, did an additional year in drug development, got a job back in

Montreal, met my husband, and ended up in San Antonio.

You couldn't really make that kind of connection. It looks all bizarre.

**You are dealing with patients who are probably the most vulnerable and underserved. It's very far from Canada.**

**AL:** You know what, I've been in San Antonio now for 26 years. It is home now. I am invested in the population, I feel very comfortable here. I am very used to the Spanish language, a mixture of Tex-Mex, the culture. It really is home. I was born in Montreal, speaking French, but the cultures are very similar in many ways.

**You are dealing with border communities, real disparities...**

**AL:** We are. Correct.

When I came here in 1992, my chief of division, Rick Parmley, had applied for a minority CCOP and got the first grant in 1990, and it has kept going since then.

We had affiliations—and still do—with Corpus Christi, and they have a fantastic outreach program and network connected to the hospital, and they have single EMR, and a transport system.

They have ambulances and planes—the hospital owns five planes.

Because there is so much distance, we have to move providers to work with the patients.

**That must be quite a territory.**

**AL:** It is quite a territory. Currently, we cover over 90,000 square miles, and it covers the entire South Texas and covers Central Texas.

With the renewal, we are adding El Paso Children's Hospital, and that basically expands the coverage area to 143,000 square miles, which is basically a little over half of Texas.

And we will be covering the entire Texas-Mexico border.

**What kind of challenges do these kids face?**

**AL:** We have COG institutions that are hubs for these patients. The biggest challenge is distance, of course, and how we get patients in.

Pediatric oncology is super-specialized in the world of medicine. The families will travel to those sites, and those institutions have housing for them.

There is Ronald McDonald, there is philanthropy that will cover it. Medicaid is covering transportation.

**In what other ways does your practice differ from anyone else's? Must be incredibly different.**

**AL:** Our patients have a lot of needs. We have a Hispanic population, and we also have adolescents and young adults.

And there is an age where resources are not as plentiful as they are for children. And that is challenging.

We do have organizations geared for AYAs. These patients have a lot of needs in terms of financial counselling to help with insurance, to help with support. It is an area of need, and it takes a lot of social worker help, a lot of case management. That gets kind of intense.

**Every doc I know has a story about a patient who taught them something about life. Who is yours?**

**AL:** They are so resilient—every patient is telling us something.

But there is one who is still in my mind. He was an adolescent, and basically a young adult. He actually was a gymnast. He had an osteosarcoma, and he lost some function of his arm.

He was able to do handstands with one arm. He got his pilot's license, and was able to move on. He actually got married to a physical therapist, who was in the military and is now in Korea.

I have this other patient, another young adult, who was diagnosed with ALL, very difficult to put back into remission. Finally went into remission with a new medication, a targeted therapy, and then went off treatment.

He almost died at induction, His family is here in San Antonio, they don't have a whole lot of money; he takes classes online. He went into remission, he actually ran a marathon in December. He has an incredible outlook on life, and he is very humble.

**How helpful is the NCORP program to you?**

**AL:** The NCORP program provides the ability to maintain a core of research personnel so necessary for conducting clinical trials.

Without that support, we wouldn't be able to open studies, follow-up patients, consent patients for study and bring access to the best treatment possible.

NCORP makes it possible for us to have enough support staff.

Also, it provides funds to allow our investigators to travel to research base meetings. It's so essential to meet with other colleagues, to trade ideas, to hear first-hand progress reports on studies we have patients enrolled on. This is essential. For those institutions, the biggest problem is not having travel money to send your investigators to your research base meetings.

NCORPs allows us to budget this money—and it has been extremely helpful and valued by all our investigators.

Also, the grant allows us to budget salary support at each site. We don't do per-case reimbursement. We realize that we deal with rare cancers. So just waiting for per-case reimbursement would not be enough to sustain the infrastructure.

The grant allows stabilization. And it has helped hospital administration to actually budget, so there is less fluctuation—and it's greatly appreciated.

## CLINICAL ROUNDUP



## CT screening reduces lung cancer mortality, NELSON study finds

Findings from the NELSON study demonstrate that the use of computed tomography screening among asymptomatic men at high risk for lung cancer led to a 26 percent (9-41%, 95% CI) reduction in lung cancer deaths at 10 years of study follow-up (at 86% compliance).

In the smaller subset of women, the rate-ratio of dying from lung cancer varied between 0.39 and 0.61 in different years of follow-up, indicating an even significant and larger reduction in lung cancer mortality than in men.

Harry De Koning, Erasmus MC, Rotterdam, Netherlands, presented these findings at the International Association for the Study of Lung Cancer's 19th World Conference on Lung Cancer in Toronto. The NELSON study was a population-based, controlled trial that enrolled 15,792 individuals, who were randomized 1:1 to either the study arm or control arm.

"These findings show that CT screenings are an effective way to assess lung

nodules in people at high risk for lung cancer, often leading to detection of suspicious nodules and subsequent surgical intervention at relatively low rates and with few false positives, and can positively increase the chances of cure in this devastating disease," De Koning said in a statement. "It is the second largest trial in the world, with an even more favorable outcome than the first trial, the NLST, showed. These results should be used to inform and direct future CT screening in the world."

Study arm participants were offered CT screenings at baseline, one, three and five and one-half years after randomization. No screenings were offered to control arm participants. Participants' records were linked to national registries with 100 percent coverage regarding cancer diagnosis (Netherlands Cancer Registry), date of death (Centre for Genealogy) and cause of death (Statistics Netherlands).

An expert panel reviewed 65 percent of cases. The follow-up period comprised a minimum of 10 years, unless deceased, for 93.7 percent of enrolled participants. The results of the study showed an 86 percent average CT screening compliance rate, encompassing 29,736 scans. In 9.3 percent of participants, additional CT scans were performed within two months to estimate nodule volume doubling time, leading to an overall referral rate of 2.3 percent for suspicious nodules.

Detection rates across the rounds varied between 0.8 and 1.1 percent, and 69 percent of screen-detected lung cancers were detected at Stage 1A or 1B. A total of 261 lung cancers (52 interval cancers) were detected before the fourth round of follow ups. In a subset of analyzed patients, surgical treatment was three times significantly more prevalent in study lung cancer patients than in control arm patients (67.7 percent versus 24.5 percent,  $p < 0.001$ ).

## Imfinzi significantly improves OS in unresectable, stage III NSCLC

Imfinzi (durvalumab) reduced the risk of death by nearly one-third compared to placebo in the phase III PACIFIC trial.

Results from the phase III PACIFIC trial in patients with unresectable stage III non-small cell lung cancer whose disease had not progressed following chemoradiation showed that Imfinzi significantly improved OS, the second primary endpoint of the trial, compared to placebo regardless of PD-L1 expression, reducing the risk of death by 32 percent (HR 0.68, 99.73% CI 0.47-0.997;  $p = 0.0025$ ).

Updated data reaffirm unprecedented improvement in progression-free survival of more than 11 months. Astra-Zeneca and MedImmune, its global biologics research and development arm, have presented data on overall survival in the phase III PACIFIC trial of Imfinzi (durvalumab) during the Presidential Symposium of the IASLC 19th World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer in Toronto, Canada. Results were published simultaneously in the *New England Journal of Medicine*.

"The five-year survival rate in this setting has historically been around 15 percent after concurrent chemoradiation therapy," said Scott Antonia, chair of the Thoracic Oncology Department at Moffitt Cancer Center and principal investigator in the PACIFIC trial. "The significant survival benefit observed using the PACIFIC regimen provides confidence and clear rationale for a new standard of care."

Summary of primary endpoints:

- The data cut-off date for first-planned OS analysis and updated PFS analysis was March 22, 2018.

- Stratified by sex, age, and smoking history.
- Confidence interval adjusted for interim analysis.
- Criteria for statistical significance at the interim analysis of OS was a p-value  $\leq 0.00274$  for OS (using Lan DeMets spending function approximating O'Brien Fleming boundary).
- Not Reached.
- Assessed by Blinded Independent Central Review according to RECIST v1.1.
- No formal statistical comparison was made because the study had achieved significance for PFS at the first planned interim analysis (data cutoff of Feb 13, 2017).

The safety and tolerability profile for Imfinzi was consistent with that reported at the time of the previous progression-free survival analysis. Imfinzi can cause serious, potentially fatal adverse reactions.

Imfinzi is currently approved in the U.S. for the treatment of patients with unresectable stage III NSCLC whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy, based on the PACIFIC trial. It is also approved in the EU, Canada, Switzerland, India, Japan and Brazil. Other global health authority reviews and submissions are ongoing.

## Tecentriq + chemo significantly improves OS as initial treatment for ES-SCLC

Genentech announced positive results from the phase III IMpower133 study of Tecentriq (atezolizumab) plus carboplatin and etoposide for the initial treatment of people with previous-

ly-untreated extensive-stage small cell lung cancer.

Genentech is a member of the Roche Group.

The analysis showed that Tecentriq and chemotherapy helped people live significantly longer compared with chemotherapy alone (overall survival = 12.3 versus 10.3 months; hazard ratio = 0.70, 95 percent CI: 0.54-0.91;  $p=0.0069$ ) in the intention-to-treat population.

The Tecentriq-based combination also significantly reduced the risk of disease worsening or death (progression-free survival) compared with chemotherapy alone (PFS=5.2 versus 4.3 months; HR=0.77, 95 percent CI: 0.62-0.96;  $p=0.017$ ). Safety for the Tecentriq and chemotherapy combination appeared consistent with the known safety profile of the individual medicines, and no new safety signals were identified with the combination.

The data was presented at the International Association for the Study of Lung Cancer 2018 World Conference on Lung Cancer Presidential Symposium. The data will be simultaneously published in the New England Journal of Medicine.

IMpower133 is a phase III, multicenter, double-blinded, randomized placebo-controlled study evaluating the efficacy and safety of Tecentriq in combination with chemotherapy (carboplatin and etoposide) versus chemotherapy (carboplatin and etoposide) alone in chemotherapy-naïve people with ES-SCLC.

The study enrolled 403 people who were randomized equally (1:1) to receive:

- Tecentriq in combination with carboplatin and etoposide (Arm A), or
- Placebo in combination with carboplatin and etoposide (Arm B, control arm)

During the treatment-induction phase, people received treatment on 21-day cycles for four cycles, followed by maintenance with Tecentriq or placebo until progressive disease as assessed by the investigator using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1). Treatment could be continued until persistent radiographic PD or symptomatic deterioration was observed.

The co-primary endpoints were:

- PFS as determined by the investigator using RECIST v1.1 in the ITT population
- OS in the ITT population

Safety for the Tecentriq and chemotherapy combination appeared consistent with the known safety profile of the individual medicines, and no new safety signals were identified with the combination. Grade III-IV treatment-related adverse events were reported in 56.6 percent of people receiving Tecentriq plus chemotherapy compared to 56.1 percent of people receiving chemotherapy alone.

## Atezolizumab + carboplatin & pemetrexed improves PFS in stage IV non-squamous NSCLC

Findings from a recent study demonstrate that the use of atezolizumab, a PD-L1 inhibitor, in combination with carboplatin plus pemetrexed as first-line therapy and pemetrexed as maintenance therapy improves progression free survival in patients with stage IV non-squamous non-small cell lung cancer.

Vassiliki Papadimitrakopoulou, chief of the Section of Thoracic Medical Oncology at MD Anderson Cancer Center,

presents these findings at the International Association for the Study of Lung Cancer's 19th World Conference on Lung Cancer in Toronto, Canada.

IMpower132 is a global, randomized, open-label, phase III study of 578 chemotherapy-naïve patients with stage IV non-squamous NSCLC. Eligibility criteria included measurable disease by Response Evaluation Criteria in Solid Tumors guidelines v1.1 and Eastern Cooperative Oncology Group Performance Status 0-1.

Exclusion criteria included tumors known to harbor epidermal growth factor receptor or anaplastic lymphoma kinase driver mutations, untreated central nervous system metastases, autoimmune disease and prior exposure to immunotherapy.

Patients were randomized 1:1 to receive four or six cycles of carboplatin area under the curve 6 mg/mL/min or cisplatin 75 mg/m<sup>2</sup> plus pemetrexed 500 mg/m<sup>2</sup> Q3W, followed by pemetrexed as maintenance therapy (Arm B), or carboplatin-pemetrexed or cisplatin-pemetrexed plus atezolizumab 1200 mg, followed by pemetrexed plus atezolizumab as maintenance therapy (Arm A).

Results of the study showed that the atezolizumab plus pemetrexed-based chemotherapy (Arm A) resulted in improvement in PFS (median 7.6 months versus 5.2 months for the control group) associated with 40 percent reduction in risk for progression (HR 0.60, 95% CI :0.49, 0.72) in all patients and across key clinical subgroups, including Asian patients (HR 0.42; 95% CI:0.28-0.63), never smokers (HR 0.49; 95% CI 0.28-0.87), current and former smokers (HR 0.61; 95% CI 0.50-0.74).

Also, at this interim OS analysis, this atezolizumab plus pemetrexed-based chemotherapy demonstrated a numerical improvement in OS of 4.5 months

over pemetrexed-based chemotherapy alone (HR 0.46; 95% CI :0.22-0.96).

These IMpower132 study results are significant because it further supports the use of atezolizumab plus chemotherapy with or without Avastin (bevacizumab) in chemotherapy-naïve NSCLC.

## Myriad's Variant Reclassification Study published in JAMA

Myriad Genetics announced that results from a landmark study of variant classifications following hereditary cancer genetic testing were published in the Journal of the American Medical Association.

This was a retrospective study of individuals who had genetic testing from 2006-2016 at Myriad Genetics. Genetic variants were classified as Benign, Likely Benign, Variant of Uncertain Significance, Likely Pathogenic, or Pathogenic. The primary objective of this study was to measure the frequency and types of variant reclassification.

The results showed that 1.45 million individuals had genetic testing in the 10-year time period and 59,955 amended reports were issued due to variant reclassification. Importantly, 25 percent of all reported variants of uncertain significance were reclassified, with 91 percent downgraded to Benign/Likely Benign and 9 percent upgraded to Pathogenic/Likely Pathogenic.

"The implications of this study are three-pronged," said Theodora Ross, senior author of the study and professor of Internal Medicine at UT Southwestern Medical Center. "Physicians need to be aware of how rapidly knowledge about gene variants is advancing and that reclassifications are common. Labs need to review gene variant information on a regular basis

and alert physicians to changes. Finally, patients and their family members need to be made aware of reclassifications by their physicians so they can make well-informed choices."

## Alunbrig improves PFS by over 50% vs. crizotinib in first-line advanced ALK+ NSCLC

Takeda Pharmaceutical Co. Ltd. announced results from the phase III ALTA-1L (ALK in lung cancer trial of BrigAtinib in 1st Line) trial, demonstrating that Alunbrig reduced the risk of disease progression or death, known as progression-free survival, as assessed by a blinded independent review committee, by more than 50 percent compared to crizotinib in adults with anaplastic lymphoma kinase-positive locally advanced or metastatic non-small cell lung cancer who had not received a prior ALK inhibitor.

Findings from the first interim analysis of the ALTA-1L trial was presented during the Presidential Symposium at the International Association for the Study of Lung Cancer 19th World Conference on Lung Cancer in Toronto. The data were also simultaneously published online in The New England Journal of Medicine. Alunbrig is currently not approved as first-line therapy for advanced ALK+ NSCLC.

ALTA-1L is a global, randomized, open-label, comparative, multicenter trial, which enrolled 275 patients with ALK+ locally advanced or metastatic NSCLC who have not received prior treatment with an ALK inhibitor but may have received up to one prior regimen of chemotherapy in the advanced setting.

Patients were eligible for study entry on the basis of locally determined ALK testing. Patients received either Alun-

brig, 180 mg once daily with seven-day lead-in at 90 mg once daily, or crizotinib, 250 mg twice daily.

Treatment with Alunbrig resulted in superior PFS compared to crizotinib as assessed by a blinded independent review committee (hazard ratio = 0.49 [95 percent confidence interval, 0.33 to 0.74]; log-rank  $p=0.0007$ ), corresponding to a 51 percent reduction in the risk of disease progression or death. The safety profile associated with Alunbrig was generally consistent with the existing U.S. prescribing information.

Research at the University of Colorado Cancer Center and lead investigator of ALTA-1L, include:

- A total of 275 patients were randomized to either brigatinib ( $n=137$ ) or crizotinib ( $n=138$ ). The median age was 59 years (Brigatinib, 58; Crizotinib, 60) and 55 percent of patients in the trial were female (Brigatinib, 50%; Crizotinib, 59%). Twenty-nine percent had brain metastases at baseline (Brigatinib, 29%; Crizotinib, 30%), with comparable pre-enrollment CNS radiotherapy rates. Overall, 27 percent of patients had prior chemotherapy in the locally advanced or metastatic setting (Brigatinib, 26%; Crizotinib, 27%).
- At the data cutoff for the first interim analysis (February 19, 2018), at a median follow-up period of 11.0 and 9.3 months in the Brigatinib arm and Crizotinib arm, respectively, 95 patients (69%) in the brigatinib arm and 59 patients (43%) in the crizotinib arm remained on study treatment.
- The trial has met the pre-specified threshold for superiority in the primary endpoint at the first interim analysis. With a total of 99 events, BIRC-assessed PFS with brigatinib was superior to crizotinib (hazard ratio, 0.49 [95% confidence interval, 0.33 to 0.74]; log-rank  $p=0.0007$ ).

- The safety profile associated with ALUNBRIG was generally consistent with the existing U.S. prescribing information.

The phase III ALTA-1L (ALK in Lung Cancer Trial of Brigatinib in 1st Line) trial of ALUNBRIG in adults is a global, ongoing, randomized, open-label, comparative, multicenter trial, which enrolled 275 patients with ALK+ locally advanced or metastatic NSCLC who have not received prior treatment with an ALK inhibitor.

Patients received either ALUNBRIG, 180 mg once daily with seven-day lead-in at 90 mg once daily, or crizotinib, 250 mg twice daily. Blinded Independent Review Committee-assessed progression-free survival was the primary endpoint.

Secondary endpoints included objective response rate per RECIST v1.1, intracranial ORR, intracranial PFS, overall survival, safety and tolerability. A total of approximately 198 PFS events are planned at the final analysis of the primary endpoint in order to demonstrate a minimum of six months PFS improvement over crizotinib. The trial is designed with two pre-specified interim analyses for the primary endpoint – one at approximately 50 percent of planned PFS events and one at approximately 75 percent of planned PFS events.

## Cancer patients have lower risk of opioid-related death than general public

Opioid use among cancer patients does not appear to be leading to the steep increase of overdoses seen in the general public, according to a study by Duke Cancer Institute researchers.

The study, presented to the ASCO Quality Care Symposium in Phoenix, found

that death from opioids are 10 times less likely to occur in cancer patients compared to the general population.

During a 10-year period from 2006-16, the researchers found that opioid deaths in the general population increased from 5.33 to 8.97 per 100,000 people. For cancer patients, the rate rose from 0.52 to 0.66 per 100,000.

In all, 895 cancer patients died as a result of opioids over that period, compared to 193,500 in the non-cancer population.

Researchers used de-identified death certificate data from the National Center for Health Statistics, which cites one underlying cause of death and up to 20 contributing causes, as well as demographic data.

All deaths due to opioids were included from 2006-2016; if present, cancer was noted as a contributing cause. Opioid death incidence was calculated from both the U.S. and estimated cancer survivor population.

## Breast cancer patients prefer knowing costs prior to starting treatment

Even when they had good health insurance coverage, women with breast cancer reported having financial worries related to their care, and the vast majority said they preferred to know about treatment costs at the time of diagnosis.

The findings from a study by Duke Cancer Institute researchers highlight the importance of considering medical costs as women face breast cancer treatment decisions.

The vast majority of women—eight out of 10—said they preferred know-

ing the costs of treatment prior to embarking on cancer care. And 40 percent preferred that doctors consider costs when making treatment recommendations.

In the study, the Duke team surveyed more than 750 women after breast cancer from the Army of Women and Sisters Network, national organizations of women after breast cancer. All were women with a median age of about 50. Most had either private health insurance or Medicare, and had annual household income of more than \$74,000.

Even within this group—financially better off than many cancer patients—nearly 16 percent reported significant to catastrophic financial burden.

Median reported out-of-pocket costs were \$3,500, although 5 percent of women faced out-of-pocket costs over \$30,000.

## CIMAvax-EGF well tolerated for NSCLC, initial findings show

Initial results from the first North American clinical study of CIMAvax-EGF show that this Cuban-developed immunotherapy is safe, well tolerated and worthy of further study. Principal Investigator Grace Dy, of Roswell Park Comprehensive Cancer Center, presented the findings at the International Association for the Study of Lung Cancer's 19th World Conference on Lung Cancer in Toronto, Canada.

The poster presentation reports results from the first portion of an ongoing phase I/II study of CIMAvax, an epidermal growth factor-depleting immunotherapy, in combination with the checkpoint inhibitor nivolumab (brand name Opdivo) in 13 patients with advanced non-small cell lung cancer. Nivolumab is an anti-PD1 antibody

and is a standard therapeutic option in many countries, including the U.S., for patients with treatment-resistant or recurrent NSCLC.

No patients experienced life-threatening side effects attributable to the combination. One patient — representing 7 percent of this small study sample — experienced an on-target grade III side effect, myocarditis, attributed to nivolumab.

Earlier studies from Cuba have demonstrated a survival benefit for patients with advanced NSCLC who received maintenance doses of CIMAvax therapy in advanced NSCLC. While this initial dose-escalation portion of the ongoing Roswell Park study did not set out to evaluate efficacy, further examinations are underway.

Dy's study was presented in collaboration with scientists from the Centro de Inmunología Molecular and Innovative Immunotherapy Alliance, a new company spun off from both Roswell Park and the CIM — the first-ever U.S.-Cuban biotech venture.

## DRUGS & TARGETS



## FDA approves Vizimpro for NSCLC indication

FDA has approved Vizimpro (dacomitinib), a kinase inhibitor for the first-line treatment of patients with metastatic non-small cell lung cancer with epidermal growth factor receptor exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

Vizimpro is sponsored by Pfizer.

The safety and efficacy of Vizimpro was demonstrated in ARCHER 1050, a randomized, multicenter, multinational, open-label study. Patients were required to have unresectable, metastatic NSCLC with no prior therapy for metastatic disease or recurrent disease with a minimum of 12 months disease-free after completion of systemic therapy; an Eastern Cooperative Oncology Group performance status of 0 or 1; EGFR exon 19 deletion or exon 21 L858R substitution mutations. A total of 452 patients were randomized 1:1 to Vizimpro (n=227) or gefitinib (n=225). The primary endpoint was progression-free survival as determined by blinded Independent Radiologic Central review, and additional efficacy

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outcomes included overall response rate, duration of response (DoR) and overall survival.

A statistically significant improvement in PFS as determined by the IRC was demonstrated for patients randomized to Vizimpro compared with gefitinib (HR = 0.59 [95% CI: 0.47, 0.74],  $p < 0.0001$ ). Median PFS in the Vizimpro group was 14.7 months (95% CI: 11.1, 16.6) compared with 9.2 months (95% CI: 9.1, 11.0) in the gefitinib arm.

“EGFR-mutated advanced non-small cell lung cancer is a common illness, especially in the Asian population, and new treatment options will ultimately benefit patients,” said Tony Mok, primary investigator for the ARCHER 1050 study and chair of Department of Clinical Oncology, The Chinese University of Hong Kong. “The findings from ARCHER 1050 suggest that Vizimpro should be considered as a new first-line treatment option for patients with EGFR-mutated non-small cell lung cancer exon 19 deletion or exon 21 L858R substitution mutations.”

Among 227 patients with EGFR-mutated metastatic NSCLC who received Vizimpro in ARCHER 1050, the most common (> 20%) adverse reactions were diarrhea (87%), rash (69%), paronychia (64%), stomatitis (45%), decreased appetite (31%), dry skin (30%), decreased weight (26%), alopecia (23%), cough (21%), and pruritus (21%). Serious adverse reactions occurred in 27 percent of patients treated with Vizimpro. The most common ( $\geq 1\%$ ) serious adverse reactions reported were diarrhea (2.2%) and interstitial lung disease (1.3%). The full prescribing information for Vizimpro can be found here.

In 2012, Pfizer and SFJ Pharmaceuticals entered into a collaborative development agreement to conduct ARCHER 1050 across multiple sites.

SFJ is a global drug development company, which provides a unique and

highly customized co-development partnering model for the world's top pharmaceutical and biotechnology companies. Under this agreement, SFJ Pharmaceuticals provided the funding and conducted the trial to generate the clinical data used to support this application.

Pfizer retains all rights to commercialize Vizimpro globally.

## FDA approves Copiktra for CLL/SLL indications

FDA has approved Copiktra (duvelisib), an oral inhibitor of phosphoinositide 3-kinase and the first approved dual inhibitor of PI3K-delta and PI3K-gamma. Copiktra is approved for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma after at least two prior therapies.

The agent is sponsored by Verastem Inc.

Copiktra also received accelerated approval for the treatment of adult patients with relapsed or refractory follicular lymphoma after at least two prior systemic therapies. The indication in FL is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Use of Copiktra is associated with a boxed warning for four fatal and/or serious toxicities: infections, diarrhea or colitis, cutaneous reactions, and pneumonitis. Verastem Oncology is implementing an informational Risk Evaluation and Mitigation Strategy to provide appropriate dosing and safety information to better support physicians in managing their patients on Copiktra.

Additionally, use of Copiktra is also associated with adverse reactions which may require dose reduction, treatment delay or discontinuation of Copiktra. Warnings and precautions are provided for infections, diarrhea or colitis, cutaneous reactions, pneumonitis, hepatotoxicity, neutropenia, and embryo-fetal toxicity.

## FDA grants QIDP and Fast Track Designations to Cidara

FDA has granted Qualified Infectious Disease Product and Fast Track designations for the company's prophylaxis development program for its lead antifungal product candidate, rezafungin for injection.

The drug is sponsored by Cidara Therapeutics Inc.

Specifically, the QIDP designation is for the development of rezafungin for the prevention of invasive fungal infections in adults undergoing allogeneic bone marrow transplantation. Cidara previously announced QIDP designation for rezafungin for the treatment of invasive fungal infections caused by *Candida*.

Cidara is developing rezafungin, a novel antifungal echinocandin, as a once-weekly, high-exposure therapy for the treatment and prevention of serious invasive fungal infections. Rezafungin is being studied to address unmet needs in the treatment of candidemia and invasive candidiasis as well as for prophylaxis of invasive fungal infections due to common fungal pathogens: *Candida*, *Aspergillus* and *Pneumocystis*.

No agent has been approved to date to prevent infections caused by these pathogens and current prophylaxis regimens often require multiple anti-

fungal drugs with safety and tolerability issues. Cidara plans to commence the phase III ReSPECT prophylaxis clinical trial of rezafungin in patients undergoing allogeneic bone marrow transplantation in the first quarter of 2019.

The QIDP designation, provided under the Generating Antibiotic Incentives Now Act, offers certain incentives for the development of new antifungal and antibacterial drugs, including Fast Track, priority review and, if rezafungin is ultimately approved by the FDA, eligibility for an additional five years of marketing exclusivity. Fast Track designation enables more frequent interactions with the FDA review team to expedite drug development.

## Blincyto approved In Japan for relapsed or refractory B-cell ALL

Japanese Ministry of Health, Labour and Welfare has granted marketing approval for Blincyto (blinatumomab) for the treatment of relapsed or refractory B-cell acute lymphoblastic leukemia. Blincyto was developed in Japan by Amgen Astellas BioPharma K.K., a joint venture between Amgen and Astellas Pharma Inc., a pharmaceutical company headquartered in Tokyo.

Blincyto is sponsored by Amgen Inc.

Blincyto is the first-and-only bispecific T cell engager immunotherapy construct approved globally. It is also the first approved immunotherapy from Amgen's BiTE platform, an innovative approach that helps the body's immune system target cancer cells.

The approval is based on data from multiple global studies, including the phase III TOWER study and Japan phase Ib/II Horai study. In the TOWER study, Blincyto demonstrated a superior im-

provement in median overall survival versus standard of care chemotherapy.

Median OS was 7.7 months (95% CI: 5.6, 9.6) for Blincyto versus 4.0 months (95 percent CI: 2.9, 5.3) for SOC (HR for death=0.71; p=0.012). Safety results among subjects who received Blincyto were comparable to those seen in the previous phase II studies of Blincyto in adult patients with Philadelphia chromosome-negative relapsed or refractory B-cell precursor ALL.

In the phase Ib/II Horai study, Blincyto was administered to 35 Japanese adult and pediatric patients with relapsed or refractory B-cell precursor ALL. The safety results from the Horai study were comparable to those seen in the global studies, including TOWER.

Blincyto is now approved in 57 countries, including the U.S., all member countries in the European Union and the European Economic Area, Canada and Australia.

The TOWER study was a phase III, randomized, active-controlled, open-label study investigating the efficacy of Blincyto versus SOC chemotherapy in 405 adult patients with Ph- relapsed or refractory B-cell precursor ALL.

The study enrolled a difficult-to-treat patient population which included patients with one or more relapses or refractory disease. In the Blincyto arm, this included 35 percent of patients that had relapsed post-allogeneic hematopoietic stem cell transplant and excluded those with late first relapse ( $\geq 12$  months after initial remission).

Patients were randomized in a 2:1 ratio to receive Blincyto (n=271) or treatment with investigator choice of SOC chemotherapy (n=134). The determination of efficacy was based on OS. These results were published in The New England Journal of Medicine.

The Horai study is a phase Ib/II, single-arm, open-label study evaluating the safety and efficacy of Blincyto in Japanese adult and pediatric patients with relapsed or refractory B-cell precursor ALL. The primary endpoint for the phase Ib portion was incidence of dose-limiting toxicities; the primary endpoint for the phase II portion was complete remission or complete remission with partial hematologic recovery within 12 weeks of treatment with Blincyto. Secondary endpoints include duration of response, OS and relapse-free survival. An extension of the study is ongoing.

## European Commission approves Coherus's Udenyca

The European Commission has granted marketing authorization to Udenyca (formerly CHS-1701), a pegfilgrastim (Neulasta) biosimilar. Udenyca is one of the first pegfilgrastim biosimilars to gain marketing authorization in Europe.

The drug is sponsored by Coherus Biosciences Inc.

Udenyca (pegfilgrastim-cbqv), formerly CHS-1701, is a growth-colony-stimulating-factor designed to decrease the chance of infection as manifested by febrile neutropenia (fever, often with other signs of infection, associated with an abnormally low number of infection-fighting white blood cells), in patients with non-myeloid cancer who are receiving myelosuppressive chemotherapy that has a clinically significant incidence of febrile neutropenia.

Udenyca drug substance manufacturing is located in Boulder, CO. Pegfilgrastim is one of the largest selling oncology biologics with worldwide revenues in excess of \$4.5 billion in 2017. Udenyca is not yet available for commercial sale.

## NCI TRIALS



## NCI Trials for September

The National Cancer Institute Cancer Therapy Evaluation Program approved the following clinical research studies last month.

For further information, contact the principal investigator listed.

### Phase I - ABTC-1701

Pilot Surgical PK Study of BGB324 in Recurrent Glioblastoma Patients

*Adult Brain Tumor Consortium*

Nakano, Ichiro  
(205) 934-1813

### Phase I/II - 10096

A Phase 1/2 Study of Combination Olaparib and Radium-223 in Men with Metastatic Castration-Resistant Prostate Cancer with Bone Metastases (COMRADE)

*Yale University Cancer Center LAO*

McKay, Rana Ramzi  
(858) 822-6185

### Phase II - 10144

A Phase II Study of Olaparib (AZD2281) in Patients with Metastatic/Advanced Urothelial Carcinoma with DNA-Repair Defects

*National Cancer Institute LAO*  
Apolo, Andrea Borghese  
(301) 480-0536

### Phase II - AMC-102

A Randomized Phase II Trial of Concurrent Chemotherapy and Pelvic Radiation Therapy with or Without Paclitaxel and Carboplatin in HIV-Positive Women with Locally Advanced Cervical Cancer (LACC)

*AIDS Malignancy Consortium*  
Ndlovu, Ntokozo  
2634791631 X 2264

### Phase II - NRG-GY012

A Randomized Phase II Study Comparing Single-Agent Olaparib, Single Agent Cediranib, and the Combination of Cediranib/Olaparib in Women with Recurrent, Persistent or Metastatic Endometrial Cancer

*NRG Oncology*  
Mackay, Helen Jane  
(416) 946-2000

### Phase III - S1614

A Phase III Randomized Trial of Prophylactic Antiviral Therapy in Patients with Current or Past Hepatitis B Virus (HBV) Infection Receiving Anti-Cancer Therapy for Solid Tumors

*SWOG*  
Hwang, Jessica P.  
(713) 745-4516

### Phase III - S1802

Phase III Randomized Trial of Standard Systemic Therapy (SST) Versus Stan-

dard Systemic Therapy Plus Definitive Treatment (Surgery or Radiation) of the Primary Tumor in Metastatic Prostate Cancer

*SWOG*  
Chapin, Brian Francis  
(713) 794-5590

### Phase Other - AALL18B3-Q

Discovery of the Genetic Basis of ALL in Children with Down Syndrome

*Children's Oncology Group*  
Rabin, Karen Ruth  
(832) 824-4213

### Phase Other - AMC-Ao4

Development of a Health-Related Symptom Index for Spanish-Speaking Persons Diagnosed with and Either Treated or Monitored for Anal High-Grade Squamous Intraepithelial Lesions (HSIL)

*AIDS Malignancy Consortium*  
Atkinson, Thomas Michael  
(646) 888-0089

### Phase Other - ECOG-ACRIN-EAQ161CD

Biomarker Testing in Common Solid Cancers: An Assessment of Current Practices in Precision Oncology in the Community Setting

*ECOG-ACRIN Cancer Research Group*  
Trosman, Julia  
(224) 619-2900

### Phase Other - WF-1801

A Single Arm, Pilot Study of Ramipril for Preventing Radiation-Induced Cognitive Decline in Glioblastoma (GBM) Patients Receiving Brain Radiotherapy

*Wake Forest NCORP Research Base*  
Chan, Michael D.  
(336) 713-3600