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HIS SIX-MONTH “LISTENING TOUR” ALMOST OVER, SHARPLESS DISCUSSES HIS VISION FOR NCI

“The notion that cancer’s not one disease, but thousands of diseases is really starting to sink in,” NCI Director Norman “Ned” Sharpless said in a conversation with The Cancer Letter, “and it means we have to change how we do everything.”

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A close-up portrait of Norman E. 'Ned' Sharpless, a middle-aged man with short, light brown hair and a friendly smile. He is wearing a dark blue suit jacket, a white dress shirt, and a patterned tie. The background is a soft, out-of-focus outdoor setting with greenery and a light-colored wall. A red banner is overlaid at the bottom of the image, containing text.

His six-month “listening tour” almost over, Sharpless discusses his vision for NCI

Norman E. “Ned” Sharpless
Director of the National Cancer Institute

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

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CONVERSATION WITH THE CANCER LETTER

“The notion that cancer’s not one disease, but thousands of diseases is really starting to sink in, and the implications of that fact are being felt throughout [NCI], and it means we have to change how we do everything. I hope that the early days of the Sharpless administration will be remembered as a time when we really bought into that reality and did some things differently,” NCI Director Norman “Ned” Sharpless said in a conversation with The Cancer Letter.

A video of the conversation is posted [here](#).

“My plan is I think the first people that need to hear about my new vision for the NCI are the intramural program and NCI staff,” Sharpless said. “So, I plan to have a town hall sometime in March, date to be determined, followed up by some sort of more national event after that where I can talk about this.

“Both at open forums, but I really want to make sure that the NCI people hear it from me directly first and have an opportunity to ask questions about it.”

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

Paul Goldberg: Thank you very much for sitting down to talk with me. How do you like the job so far?

Ned Sharpless: So far, so good. I’m enjoying the new job greatly. The colleagues are wonderful, the sense of mission at the National Cancer Institute is very strong, and so, working with people who are so talented and so passionate is really a privilege.

My guess is that you’re playing a long game rather than a short game, so 10 years from now, when we all look back at the Sharpless years, you may still be there—or here, rather—what do you want people to say?

NS: I think you’re right about that. The NCI lends itself to gradual change and the nature and size of the culture and the institution is such that the long game is really the way to go. I think it is likely what we’ll say 10 years from now is that this is a time when things were really changing in cancer research.

This notion that cancer’s not one disease, but thousands of diseases is really starting to sink in, and the implications of that fact are being felt throughout the institution, and it means we have to change how we do everything. So, I hope that the early days of the Sharpless administration will be remembered as a time when we really bought into that reality and did some things differently.

And then what happens?

NS: We’ll have to change how we do clinical trials. We’ll have to change how we even hope to gain further knowledge in cancer research. So, for example, I’ve spoken a lot about my belief in the power of Big Data and data aggregation.

The reason I’m fervently passionate about that idea is that it really is one of the only ways that we can make some of the progress I hope to make by—if it’s a thousand diseases, some of those diseases are quite rare, and so the traditional paradigm of a 500-patient clinical trial doesn’t work so well in the new reality of fragmented cancer diagnoses and instead what we’ll need is large aggregated data sets to see and discover the behavior of those sorts of tumor types. Those will inform basic biology, cancer disparities research, survivor research. You know, whatever your interest is in cancer, it’s addressed by aggregated, annotated data sets.

What role should NCI play in bioinformatics? What should you do? What should the industry do?

NS: Well, I think that’s right that there are a number of players in this field that have an important role. I think the National Cancer Institute’s particular role—it can fund research and play a role in standard setting so that if a bunch of different industry players develop different sort of data silos that don’t work together, that doesn’t really advance the research mission to the extent we would like.

I think the NCI can say, “If you’re going to get data elements from an electronic health record, these are the ones you

should get in this format. If you're going to use a sort of strategy to uniquely identify patients, here's one that works. If you're going to store data in certain formats, here's a good way to do it so that they can be aggregated and talk to each other."

I think that we have a role to play in standard-setting and incentivizing the top research. If you have these huge data sets, how do you mine them? You can't use your Excel spreadsheet and click on "sort" or whatever for terabytes of data, so making sense of those large data sets is going to require a significant research effort.

I think that that's probably a better fit for us than trying to create the uber, all things, ginormous, Skynet-type data bank. That, I think, would not be a good idea, because that would preclude innovation. That would prevent the different small companies from doing what they're doing and the academic entities from trying to develop new structures.

So, I think facilitating research and letting this grow organically and trying to figure out and identify the winners and then force them to work together and aggregate is really a useful role for the NCI.

Is that more of an honest broker role, or is it more of a standard-setter, in a kind of more planning sense?

NS: We certainly can play both of those roles. We have an important honest broker role for example in the [Surveillance, Epidemiology, and End Results Program] dataset, where we hold a lot of de-identified data from multiple different SEER contract sites and make that available to the research community. We similarly have a very important standard-setting role that I alluded

to, but I think it's a lot more than just those two functions.

We also have a research role of identifying the key scientists working in data science and saying, "If we make these sort of datasets available to you, how are you going to use them? What are you going to do with them?" So, I think the research efforts are really important. And, similarly, I think we have a, for want of a better term, a sort of role in data quality assurance in the greater world so that we want to provide large sets of data that we know to be of very high quality, they're properly annotated and linked that can then be used by the research community for particular endeavors.

The Genomic Data Commons, for example, is not merely a repository of data that the NCI runs, but it's also a repository of quality, validated data that can be used for these research efforts.

One of the most interesting stories I'm covering now, I think, is the spread of the academic model into the community setting. How does that affect NCI? What should you be doing differently? Is there anything you need to be doing differently?

NS: Yes, I agree with you. This is a really important development and a really big story nationally. I think it makes total sense once you realize that cancer is thousands of diseases. No single institution is going to have enough of these certain rare subtypes to really do meaningful clinical research so multi-institutional studies is the next thing that happens, but that only takes you so far and pretty soon, you realize you're going to have to do clinical trials and translation of best practices in the community setting.

That's where things are going, I agree. The ability to do enrollment into clinical trials at community oncology practices is a big new development, and the ability to do sort of cutting-edge research and translate novel therapy in the community setting is a big development. It's good for patients. They don't want to drive three hours to the cancer center.

It's good for research, because clinical trial enrollments in adult oncology is about 3 to 5 percent of patients and I think the only way we're going to make that better is by enrolling patients in the community oncology setting. So, it's good for patients, it's good for research, and I think community oncologists like it. They don't want to have to refer patients for tertiary care. They prefer to keep patients home and under their care.

So, I think it's a win-win-win, but how to make it happen? As you know, the National Cancer Institute has a big investment in the so-called National Community Oncology Research Program, NCORP. That is an entity that is a very successful program that we have pledged new investment in, so, we plan to grow the NCORP. It's where a lot of the research for the NCI-MATCH, meaning the patients on the [Molecular Analysis for Therapy Choice] trial were enrolled at NCORP sites, and similarly, it's a great fit for certain kinds of research like the TMIST trial, which is this mammography study that will be done over the next seven years.

Not every trial works in the NCORP setting, but some work really, really well. I think that a commitment to continued research in the community setting and figuring out how to grow that and figuring out how to do a more diverse set of trials in the community setting are future challenges.

As I look at this—and I can only look at it as a reporter, but you're a former cancer center director and you're now the NCI director—what does all of this, all of the things you've just described do to the definition of a cancer center? Does it need to be redefined? Maybe this is a premature question to ask.

NS: No, no, I think it's a good question. I don't think the move to do more care closer to home is in any way a threat to cancer centers. I think that most cancer centers have fairly large catchment areas, in fact, and are really challenged by the NCI to figure out how to do research throughout the patients in their entire catchment area. So, they've all, many of them have started thinking about how to use satellite facilities or how to collaborate with more local partners.

I think this, as I said, makes sense, because cancer centers are very much judged on the metric of incident number of cases, enrollment to clinical trials and sort of novel research efforts and, to do that in the modern era of thousands of different diseases requires outreach.

I don't think any sensible cancer center feels like the old days where everybody drove three hours to see them is the model going forward.

What about clinical trials? What kind of clinical trials should NCI do? What kind of clinical trials, more importantly, shouldn't NCI do? What should the role for the industry be? Where's the line between the industry and NCI? Where should it be?

NS: Yes. Industry has a huge role to play in this, and certainly significant resources to develop to address this question. Industry doesn't do certain kinds of trials where there are important research questions and I think that's really where NCI plays its most critical role.

So, for example, the willingness of pharmaceutical companies to test their drugs in pediatric populations has been probably, I would say the appetite has been lower to do that than in adult populations. So, leadership in pediatric oncology has been an important thing for the NCI to do.

Similarly, if you think about it, there's a lot of incentive for a pharma company to test their new drug, their new molecular entity, but there's less incentive for them to test new models of surgery or radiation oncology. So, those kinds of trials, multi-modality trials that involve surgery, radiation, and chemotherapy are a good fit for the NCI.

There are a lot of challenges to the modern clinical trial operation. Nothing has felt this reality of the many different kinds of cancer fact more than clinical trials, because the old paradigm was relatively simple, from an administrative point of view. You randomize 500 patients one way or the other. That's a pretty simple structure.

But now what happens is some of the lung cancer [patients] come in, they

get sequenced for 400 genes. If they have this one event, they can go in this trial. If they have another event, they can go on that trial. So, there's this huge burden of patients that are screened and not even treated, but there's still costs and expenses with those trials. The per-patient costs for accrual are much higher.

So, the clinical trials enterprise has really had to adapt and modernize, and it has not finished with that process. It is a bit painful and has caused the process to go more slowly than we would like in places, but I think there's pretty uniform agreement now among the really good clinical trials in the United States that things have to change and that what the vision of the future looks like is, I think, coming into focus.

For years now, really for many decades, the glib thing to say has been, "Here's how you free up some NCI money. Kill the intramural program. Get rid of Frederick. What have they ever done?" I'm not sure that argument holds water anymore, with HPV and with CAR-T. What size and role do you see for the intramural research program and what size and role do you see for the Frederick lab?

NS: Yes. Several things to talk about there. So, as a long-time veteran of the extramural program, I have heard this statement. I would be disingenuous if I pretended that no one had ever said anything bad about the intramural program. Having said that, even before I got here, I think I had an appreciation for the quality of the science that goes on intramurally and now, as NCI director, I really have really become very impressed.

One thing to know is that the science effort, the clinician scientists and basic scientists within the intramural program, that number has shrunk significantly over the last decade. It's now 270 scientists. We've looked on an analysis using hard metrics, publications, patents, citations by clinical trials of that cohort of scientists, and if you compare those NCI intramural clinician scientists and basic scientists to any group of extramural researchers, they compare very favorably.

I mean, they're an awesome group of scientists. It doesn't—you know, 275 people—they don't work on everything, but they work very, very well on certain topics. You alluded to HPV. I believe the world's leading HPV research has gone on here in the intramural program, led by Doug Lowy, my predecessor and deputy and wonderful sherpa in this endeavor.

I think the CAR-T effort, Steve Rosenberg [chief of the Surgery Branch, senior investigator, and head of the Tumor Immunology Section at NCI's Center for Cancer Research] work, has been transformative, and is now starting to see realization and FDA-approved therapies. Marston Linehan [chief of the Urologic Oncology Branch and senior investigator at NCI's Center for Cancer Research] has done this marvelous research on familial genitourinary cancer that's been fantastic.

There's also the intramural health services research arm, the Division of Cancer Epidemiology and Genetics, that is a national treasure. They do kinds of work that is just not doable anywhere else in the world, looking at the role of sort of types of occupational exposures and carcinogens and cancer risk, aggregating enormous data sets for GWAS [genome-wide association] studies, doing very elegant research on both survivorship and cancer therapy in the real world. It's an effort that is terrific and I think of great value and easy to defend.

Frederick is a different thing. Frederick National Lab is not really part of the intramural program, although it supports intramural research. Frederick has existed since the days of the National Cancer Act, has gone through some iterations and I think it was Dr. Harold Varmus, who decided that if we were going to have a national lab in Frederick, Md., that it had to be awesome, that it had to be really, really great and he invested both the finances and the administrative discipline to try and transform Frederick. He set it on a very good trajectory that I believe continues today.

Frederick now does some very exciting cutting-edge research like the RAS Initiative. It has these very important support capabilities that are quite marvelous where you can spin up assays and new therapeutic production facilities there in a very short time, at least for federal academia standards. I think Frederick is a valuable entity.

It has new leadership with Ethan Dmitrovsky, who I think is a very good person to play a role in leading Frederick, and I believe that Frederick is great, but we have to continually ask what can it do, and what should it do, and how can we use its special capabilities most optimally? And so, we spend a lot of time thinking about new things for Frederick to do.

Should both of these entities, maybe they should or shouldn't be grouped. Sorry if I was unfair. Should they be roughly where they are? Should they grow? Should they shrink? Or is this a premature question to ask?

NS: No, I think the intramural program has shrunk, and it's probably gotten to a size that makes sense. The clinical

enterprise here, intramurally, should not get any smaller. In fact, I think probably should be a little larger—not 50% larger—10% larger. There are some areas where we need to do some recruitment. The research enterprise, I think, is a good size. It's certainly big enough to feel like it's a dynamic environment where they're wonderful collaborators. It feels like any sort of academic research program in the country, but yet not so big that it's diverting resources away from the rest of the extramural world.

I think Frederick is a different animal. The size of Frederick depends on what Frederick is doing. If we figure out for Frederick to do new things we might increase capacity up there and if we pare back some of the activities we might see decrease in Frederick's size. Right now, the portfolio of Frederick I think is pretty strong.

The RAS Initiative is very good, some of the other efforts related to... There's a GP facility that does important production of therapeutic modalities for people at the NCI, there's a nanotechnology catheterization lab, there are a bunch of capabilities that support the intramural program. It's doing a bunch of useful things that I think are strong.

In fact, one of the things I'm most excited about Frederick is we're building this sort of cryo-EM support facility, because we have appreciated that cryo-electron microscopy is so important nationally, but a lot of places, even though they're buying and investing in the technology, really still aren't able to solve structures to the level of detail that they would like and so the NCI is a facility where people can now send us their matrices, their lattices and we will do some of the imaging for them and then help them with the data interpretation, which I think is a well-used resource and is going to grow a lot.

At the most recent National Cancer Advisory Board meeting (The Cancer Letter, Feb. 16) you spoke quite a bit about the RPG pool and the size of it and how it should be structured. It was a long and interesting discussion. If you were to summarize what the issues are and what the outcome is, if there is an outcome, what is it?

NS: Yes. The Research Project Grant pool, or the RPG pool, is an acronym I didn't understand until recently—it's one of many—is the pool of money whereby the NCI supports investigator-initiated science.

So, for the most part, it's not completely exclusive, but for the most part, RO1s and PO1s and some of the UO1s, the grants that an investigator, working on their own, dreams up in the outside world and says, "I'd like a million or \$2 million to work in this area," and applies to the NCI, that's where it comes from.

I would argue it's been a good investment, that some of the most important advances in cancer research have come from investigator-initiated science funded through RO1s, through individuals. But it's an expensive pot of money, so of the sort of \$5.6 billion NCI budget, roughly \$2 billion goes to the RPG pool and that's for \$500 million-ish for new awards, for competing and new awards, and then the rest, \$1.5 billion for renewals, because the grants are typically four to five years, non-competing awards.

So, whenever we fund a grant, it has four out-years as well, generally. Decisions we make in the RPG pool, even if they're quite small in size, like we'd like to increase everybody's grant from—typically on the non-competing

awards we would cut them a little bit, so, instead of funding them at 100% we'd fund them at 98% or 94%.

So, a couple of percentage points in the RPG pool turns into \$15 million to \$100 million annually. So, even minor decisions to the RPG pool have big implications for the NCI budget in the present year and for future years.

Against that backdrop, we have looked at the trends of the rate at which people are sending us new grants and that has gone up sharply over the last few years. We have a lot of people with great ideas in cancer research, they're sending those proposals to the NCI, and we want to fund them. But if you get more awards and you don't put in more money, then the paylines go down. That is very frustrating for the extramural community. I lived that. I know all about low paylines.

It's a tough message. If the Congress is giving us more money and we have the Moonshot funding but paylines are going down, that seems somewhat discordant. So, we have wanted very much to preserve pay lines but to also fully fund grants at 100 percent for a variety of reasons. These small little cuts that we've been imposing every year add up. We take a big cut in the beginning of the grant and then small little cuts every year and it is very frustrating to the extramural community as well. So, we're trying to preserve pay lines and fully fund non-competing renewals.

Two laudable goals that I think everybody in the extramural community would like; I proposed to our advisory board that we do that. That is something internally we've talked about among our senior program leaders and there is enthusiasm to do that within the NCI. As I said, the belief that the RPG pool is a good investment is pervasive throughout the in-

stitution, but we also wanted to sound out that with our advisory boards. And they were basically enthusiastic. They thought that these cuts really are detrimental to science, that to the extent possible, we should fund grants fully when able, that we should try and preserve paylines.

So, what that translates to in reality, though, is about \$125 million more for the RPG pool this year. That's kind of a one-time thing. It won't go up that much every year, but because of a bunch of things—out-year commitments made in prior years—this year is a particularly striking year. I don't think we would put \$125 million in the RPG pool every year, but that's what it means for this year. So, we would like to do that.

We'll know if we'll be able to do that when we learn what our budget is, 2018 enacted budget is from Congress, which we do not know yet. We are hopeful that we'll be able to put significant additional resources to the RPG pool this year.

That's fascinating. So, you're saying that the RPG pool should overall stay where it is.

NS: Or even, it actually grows a bit. I think it does, the con is that it does decrease our flexibility in 2018. And, of course, if we fund more grants this year, then those grants have out-year costs as well, so, it limits our flexibility this year and in future years. So, it's not something that we take lightly. There are a lot of things that we could do with those funds if we didn't use them for the RPG pool.

As I mentioned at the board meeting, I've asked my senior program leaders for new ideas and what they would cost, and I've met with each one of the

divisions and centers independently and gone through their budget and their future budget, and I've been proposed \$300 million of new great ideas. There's no shortage of good stuff to do, so, if we didn't use the RPG pool money for that, we could do some of these other ideas.



What may be convenient for extramural researchers or good for the intramural program or fortunate for the NCI director, none of that is as important as does it or does it not improve our success against cancer in this sort of fight against cancer for our patients.



But I think the RPG pool is sufficiently important and the preservation of that fund is sufficiently important to the extramural community and cancer research engine in general, that that's sort of got to be priority number one this year.

And that may stay that way for a while?

NS: Well, like next year we envision more flexibility. Next year we would

have to put additional money into the RPG pool again, but it would be much less. It would not be this size. It would be more like \$50 million.

If we had the same kind of budget in 2019 that we might get in 2018, then we might be able to do other things. Of course, now we're talking about the hypotheticals of congressional funding more than 12 months away, and that's bad. That's hard to do, right?

Let's not do that. So, you've mentioned that you've been on a listening tour that began in the summer and it ends in March. Which day in March, so we can all mark our calendars? How will you know?

NS: I don't know the exact day. I'll explain how I envision this. It really started before I was sworn in. I was able to go around and meet with a lot of people, but because of laws about things that you can tell a non-federal employee, I really couldn't begin it in earnest until I was sworn in October 17. So, I felt like six months was about the right length of time.

I think I'm feeling now that I am comfortable in meetings. I know what most of the acronyms stand for. I know who everybody is, so I feel like now I'm having not just information receipt, but I'm actually able to make decisions and I think the nature of the institution, if I extended it much longer than that it would probably start to frustrate people. I need to at some point to become a little more definitive about my goals for the NCI.

My plan is, I think, the first people that need to hear about my new vision for the NCI are the intramural program and NCI staff. So, I plan to have a town hall sometime in March, date to be de-

termined, followed up by some sort of more national event after that where I can talk about this. Both at open forums, but I really want to make sure that the NCI people hear it from me directly first and have an opportunity to ask questions about it.

Can you summarize what you've heard during your listening tour?

NS: Wow. That's challenging. It borders from the incredibly weedy but important, like how SEER works, or how the RPG pool works, or how Frederick works. Some of these things have, you know, Frederick has a lot to do with the occult practices of government accounting, government contracting, so it ranges from stuff like that that's very, very important but I would be hard pressed to, I think I would bore the room to tears if I were to try and explain some of those details.

But ranging to the what should the future of cancer research be? The very big picture—what are we doing right? What are we doing wrong? Where do things have to change and how can we do things faster? Really, I think one of the most important parts of that conversation, frankly, for the bigger picture stuff, has been with the patient advocates.

They've really argued that patients have to be the north star of this endeavor, that we really have to keep in mind what's best for patients with cancer to reduce the burden of cancer through prevention and screening, early detection and therapy. What may be convenient for extramural researchers or good for the intramural program or fortunate for the NCI director, none of that is as important as does it or does it not improve our success against cancer in this sort of fight against cancer for our patients.

You're talking about people who knocked on your door and came to see you, or are you talking about people located for you through the NCI advocacy outreach program?

NS: A lot of both. I've answered a lot of email. I've had brunch at Silver Diner in Bethesda with a granddad who wanted to tell me about his grandchild who died of glioma. I've met with organized advocacy groups.

Just the passion around cancer among survivors and advocates and family members and loved ones is just unbelievable. Until you've sat with these people and asked them what frustrates them and what they'd like to see the NCI do better, that exercise has proven phenomenally informative.

How's that different from what you heard as a clinician and as a center director? Is that a different level?

NS: No. That's a good question, because actually I thought I knew. I have this joke that I like to tell that my wife and I lived together before we were married and we thought we knew what marriage was like. Then when we got married, we realized, "Are you going to make that noise with a spoon for the rest of your life?"

So, I thought, doing cancer one-on-one as a doctor, I had learned a lot about the burdens of a specific patient one at a time. As a physician you try and often talk your patients into therapies that have a lot of toxicity and have both side effects and benefits and it really involves knowing that particular patient and what they want in terms of what's

the right decision. Often it's not so much medical as patient-tailored.

So, I had had that sense of individual one-on-one with patients of leukemia for a long time, and then as a cancer center director, I think the scope of reference increased substantially. But still that was really focused around the patients within a specific hospital or a specific catchment area. The things that were really good at the University of North Carolina were areas of particular focus, for example.

But now, as NCI director, there's, sort of, no kind of cancer in the United States that I can't be interested in. There's no issue around cancer, be it prevention, survivorship, Big Data usage, therapy, prevention, all of those things are important and have to be balanced, because everything has trade offs. This kind of increase in the scope of interest has been quite striking and surprising, in a good way.

And advocates are probably some of the most well-informed people about science, too, because they're kind of generalists.

NS: No, I think that's true. I think some of these advocates have worked in certain areas for 10, 20 years and they have learned everything one can learn about the cancer that interests them and they are quite sophisticated in some instances.

So, the listening tour is over, almost. We will find out when. What comes next?

NS: In the near future, what I expect to happen is we will sort of begin to focus

on a few specific areas. I've been sort of adopting this three-bin philosophy. There are things that we have to do, like the clinical trials endeavor. I alluded to this, that it works, but it needs some structural changes to make it work as well as everyone would like. There are things that we would like to do. There are areas of new effort, new investment for the NCI and that's particularly fun to think about as a new director.

And then there are things that we're already doing that need continued to significant investment. Those can be kind of nice. A prior NCI director told me, "One of the good things about the job is you get to take credit for what your predecessors did," and so, some of these great programs have been going on for years, but they're coming to fruition in the next few years. They'll be important to our cancer research endeavor.

So, that's sort of the three bins and we have plans for all of those. It involves making choices. If the budget only goes up a little bit and we have a lot of new ideas, then that means that we necessarily have to stop doing some things or increase efficiency, which I also am eager to try and do. And that has, by the way, been a strong signal from this administration.

The secretary of Health and Human Services and the White House have both sent the clear signal to the NIH that they like the NIH, they value biomedical research, but they want it to be done in an efficient and competent manner and so, there will be emphasis on that as well.

Well, thank you. I'm looking forward to covering all of this.

NS: Thank you for the pleasure of sitting down today.

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

A



CONVERSATION WITH
THE CANCER LETTER

UT Health San Antonio's link with MD Anderson goes live; How does it work?

The affiliation between UT Health San Antonio Cancer Center and MD Anderson Cancer Center became active on Feb. 20. “Administratively, the two institutions are distinct. Patients will be cared for by the physicians and nurses of the [San Antonio] Mays Cancer Center, but certainly the platform of the care that they’re being provided has been heavily informed and integrated with MD Anderson, based on their treatment templates and methodology,” Ruben Mesa, director of the Mays Cancer Center, said to The Cancer Letter.

“That platform of care is comprehensive and includes, for example, the training of the nurses, the intake process, how we’re trying to organize our supportive care programs. Even down to detailed aspects, such as the QA on the LINACs for delivering the radiation therapy,” Mesa said.



Ruben A. Mesa, M.D.,

Director of the Mays Cancer Center, the newly named center at UT Health San Antonio MD Anderson Cancer Center

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

Paul Goldberg: Can you walk me through the announcement?

Ruben Mesa: The affiliation between UT Health San Antonio Cancer Center and MD Anderson Cancer Center was announced in the fall of 2016 and we went live on Feb. 20. 'Go live' simply means that on Feb. 20, we began operation as the newest partner in the MD Anderson Cancer Network. We completed renovations in our Patient and Family Welcome Center, expanded our pharmacy and updated our chemotherapy infusion rooms, which were improvements we wanted to make before we began operations as the UT Health San Antonio MD Anderson Cancer Center.

One of our most exciting and important announcements took place on Jan. 30. One of our longtime supporters, the Mays family, pledged a legacy gift of \$30 million to support our cancer center through their Mays Family Foundation. So, our cancer center will now be known as the Mays Cancer Center, the newly named center of UT Health San Antonio MD Anderson Cancer Center.

One of the things that was necessary to get this off the ground was to have a new director, as there had been a search for a new director for almost a year. I came in at the end of August of 2017.

There were some aspects of change that had been going over in the past year during the search for the new director, but many needed a director in place to really be able to move forward. We expect the affiliation to be in place by mid-year, where the affiliation relationship is operational on a day-to-day basis regarding providing a joint program of care.

Could we focus on the mechanics of that approach, what happens? Somebody comes into your center, what happens? How does that work through MD Anderson?

RM: Administratively, the two institutions are distinct. Patients will be cared for by the physicians and nurses of the Mays Cancer Center, but certainly the platform of the care that they're being provided has been heavily informed and integrated with MD Anderson, based on their treatment templates and methodology.

That platform of care is comprehensive and includes, for example, the training of the nurses, the intake process, how we're trying to organize our supportive care programs. Even down to detailed aspects, such as the QA on the LINACs for delivering the radiation therapy. So, it's aligned along those levels.

Additionally, we've been developing a navigation system to help our patients find their way around our buildings. We recognize that some of our patients will be several hours away from San Antonio and that they may need to get some of their treatment in Houston, although our goal is for patients to receive all of their care here, close to home. Perhaps some will get a resection, proton beam or CAR-T therapy in Houston but they will get radiotherapy or chemotherapy at our center. I think there will be unique aspects of care, a small subset of patients who will be going in both directions. Still, our main goal is so that the vast majority of patients will be able to remain in San Antonio for their complete cancer care and will benefit from our joint program.

In San Antonio, have a very deep bench. We have all of the surgical disciplines, very good pathology, excellent radiol-

ogy, outstanding HemOnc, RadOnc, etc. So, we have a complete team here. A lot of the effort has been devoted to growing our team, weaving the team together, and trying to do so again with a lot of the lessons that have been learned by MD Anderson's experience in delivering great cancer care.

You just got a \$30 million gift from the Mays Family Foundation. What will that do?

RM: The gift is great on a variety of levels. The gift itself is meant to help us on the journey to growing to become a comprehensive cancer center, and advancing cancer care in San Antonio. The gift will help empower key recruitment efforts in the following areas:

- One, in cancer epidemiology and population science, to leverage and study that unique Hispanic majority population here in San Antonio.
- Two, we are working to reinvigorate early drug development and what early drug development is going to look like for the future with cellular based therapies, immune-based therapies, etc.
- Three, we have deep interest in growing our expertise in DNA repair and translating those discoveries to the clinic.

Our new dean that started last week for our university, at UT Health San Antonio, is Rob Hromas (dean of the Joe R. & Teresa Lozano Long School of Medicine at UT Health San Antonio and vice president of the university for medical affairs). Rob was former deputy director of the cancer center in New Mexico and then was the chair of medicine at the University of Florida at Shands. He too will be a strong partner in developing our efforts in cancer. He is a DNA repair expert.

We also have a really deep bench in epigenetics, so translating therapeutic opportunity of DNA repair and epigenetics will be an important focus.

How does that fit in with the MD Anderson program? You're a part of the MD Anderson outreach? I think you might be the only NCI-designated center that's in their program network?

RM: Correct. So, the relationship initially is focused very specifically around our practice collaboration. However, I know we eventually will be collaborating in research. And I think that there will be areas, as (MD Anderson President) Peter Pisters and I have discussed, that are yet to be defined.

I see opportunities based on population health, focused on the people of Texas. The MD Anderson network has national partners and state-based partners, but our affiliation came as a plan by the chancellor of The University of Texas System, Chancellor (William) McRaven, who wanted to see greater connection and collaboration between the cancer programs in the UT System. Our center, Galveston, UT Tyler, to start with, are having much deeper relationships in the practice of cancer care.

Will you be connected through Epic with MD Anderson? Will you be connected in any other way with them? How does the bioinformatics aspect of it work?

RM: We have our own distinct Epic account, but we are able to share records through Epic, and we certainly have many things that we have developed

to work together on in Epic, ranging from exact chemotherapy regimens, to everything ranging from distress assessment, to survivorship care plans, to other components.

As with all these issues with the EMR, there are many layers to it, but I think this is a big opportunity. And with the Mays Cancer Center being much smaller, we're trying to leverage a lot of MD Anderson's experience and excellence in care into our teams for the delivery of care.

I found the MD Anderson team to be incredibly engaged and helpful partners. And their experience, as in having had these relationships successfully at a variety of centers like Banner, Cooper, and even their own Houston presence. They've learned their model well in terms of which aspects of their care delivery platform are exportable and how to integrate in a new system in a way that really makes care more uniform, high quality and accountable.

What's the rationale—and the history—of your aligning with MD Anderson?

RM: Bill Henrich, the president of our university (UT Health San Antonio) has a strong passion for reinvigorating the cancer center. He is a survivor of a haploidentical transplant, so he takes this work very, very seriously. It's a center with a deep history in drug development, in breast cancer, in the potential for impacting the understanding of cancer in Latino patients, in particular, Hispanic patients, which are the majority of patients in our catchment area. He saw this affiliation as the opportunity to grow and integrate the practice and to have a model of care so that individuals would not have to leave San Antonio for their cancer care.

And now we can combine the strong research mission and tradition of the Mays Cancer Center with the MD Anderson model of patient care to really create and evolve into a center that seeks to be comprehensive in research, education and cancer care, educating the cancer providers of the future and the cancer investigators of the future and, in particular, to have a strong regional focus of excellent cancer care for the people of San Antonio and South Texas.

The catchment area of our Mays Cancer Center is a fairly sizable, expanding from San Antonio south, all the way down to Brownsville, and west, over to Laredo.

Are you going for comprehensive designation, ultimately?

RM: That's certainly our long-term goal. I don't think, for our next renewal, necessarily. But that certainly is the goal and the mission.

That was why you came to San Antonio?

RM: Correct. Clearly, what interested me, one, was the opportunity to build and augment something that has had a tremendous history. I think the bones were very strong, there was a lot of great research, there is about \$45 million in extramural funding, there are three solid NCI programs here, with potential to grow more.

There's a program in cancer development and progression, there is a program in experimental and developmental therapeutics, and that includes the historical Institute for Drug Development, our phase I program, that Dan Von Hoff founded many years ago.

And then there's our population science and prevention program that includes a real focus on issues of cancer in Hispanic patients. Later this month, Feb. 21-23 to be exact, Amelie Ramirez, who is one of the senior members of the Mays Cancer Center and focuses on cancer prevention and health promotion, is holding a national meeting on the issues of cancer in Latinos in San Antonio. Amelie is associate director for diversity and a National Academy of Medicine member who focuses on behavioral science interventions for Hispanic patients.

Folks from the NCI, folks from all around the country that are interested in this area are all coming to speak. Again, this conference will give us a lot of opportunity to compare and contrast issues between these populations. Within Hispanic populations there are some fairly sizable genetic differences and cultural differences that are relevant. This will include Hispanics from the Caribbean, kind of my family-type folks—my family is Cuban—to a Tejano population, to those who've come much more recently from Mexico. [See related story on [page 19](#) in the *Trials and Tribulations* column in *The Clinical Cancer Letter* section.]

Covering the Mays Cancer Center and related entities over the years, one of the main problems has been the absence of hospital beds to make a difference to finances of the institution. Is that being fixed? Does it need to be fixed?

RM: I think what has lacked has really been a good integration of the practice. I do think that, for the longer term, we need to explore how to better integrate our inpatient footprint. Right now, its spread between several hospitals in the San Antonio area.

In San Antonio, the majority of the medical community is there in what we call the South Texas Medical Center, where a variety of institutions are based. That includes my institution, UT Health San Antonio, our major clinical partner, University Health System, run by the county, but it is a separate institution. There are also patients that are cared for at a variety of other in-patient venues: CHRISTUS Santa Rosa, St. Luke's Baptist, Methodist.

Do you need to build a new hospital? Is that the plan?

RM: I think that there's no plan at the moment to do that. I'd say that the inpatient footprint certainly is being looked at and discussed, but certainly hope to make it more cohesive than it exists at the moment.

Is there anything we've missed?

RM: I think it's an exciting time. I'd say that keys areas we're looking grow and focus on scientifically are cancer in Hispanics, new drug development and clearly, DNA repair, epigenetics, and to be a strong resource for the people of San Antonio. As they say, it really kind of goes back to President Henrich's experience, where he had to go to Houston for a lot of his care and he realized that, for a lot of people in San Antonio, most individuals don't have the resources to be getting care away from their homes. We seek to be the key comprehensive cancer center for the people of San Antonio and the people of South Texas.

Well, thank you so much.

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Clearly, what interested me, one, was the opportunity to build and augment something that has had a tremendous history. I think the bones were very strong, there was a lot of great research, there is about \$45 million in extramural funding, there are three solid NCI programs here, with potential to grow more.

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IN BRIEF



Frederick Schnell named to new post of COA medical director



Frederick Schnell was named medical director of the Community Oncology Alliance.

In this newly created position, Schnell will focus on issues related to oncology payment reform.

Schnell was a practicing community oncologist for 34 years, most recently as CEO, at Central Georgia Cancer Care

in Macon, GA. He is a clinical assistant professor, Department of Medicine, Mercer University School of Medicine, Macon, GA. and a clinical assistant professor of hematology and oncology at the Winship Cancer Institute, Emory University School of Medicine.

Schnell has been the recipient of the Distinguished Cancer Clinician Award from the Georgia Cancer Coalition. He was a founding physician of COA, and has served as the third COA president, and as a member of the COA Board of Directors for many years.

“This is a crucial time for community oncology,” Schnell said in a statement. “There are obstacles and issues, to be sure, but the future is so much more positive and COA has more resources than at any time in its history.”

Richard Barakat to lead Northwell Health cancer services, research



Northwell Health has appointed Richard Barakat to lead its cancer services and research.

A surgeon and clinical investigator who specializes in robotic and lapa-

roscopic treatment of uterine cancer and radical debulking procedures for ovarian cancer, Barakat will serve as physician-in-chief and director of the Northwell Health Cancer Institute, senior vice president of the health system's Cancer Service Line, and professor of obstetrics and gynecology at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell.

He will also work closely with Cold Spring Harbor Laboratory as part of a strategic affiliation with Northwell on future cancer research and treatment collaborations.

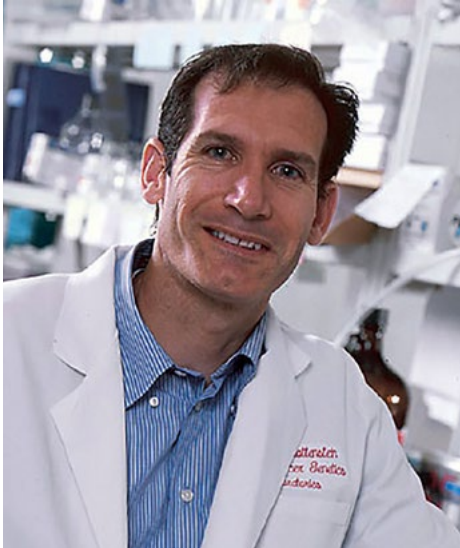
He will join Northwell on April 30 after 27 years at Memorial Sloan Kettering Cancer Center, where he served as director and vice chair of MSK's regional care network and affiliations, and the Ronald O. Perelman Chair in Gynecologic Surgery.

Throughout his career at MSK, Barakat oversaw the care of thousands of patients who were newly diagnosed with gynecologic cancer. He also served as chief of the gynecology service from 2001 to 2013 and was the lead investigator on several influential research projects, including a study to compare the benefits of laparoscopic versus standard surgery for patients with endometrial cancer and an NIH-funded study evaluating risk factors for the development of symptomatic lower-extremity lymphedema in women undergoing radical surgery and lymphadenectomy for gynecologic cancer.

Barakat was a division member and examiner for the American Board of Obstetrics and Gynecology and vice chair of the Cancer Prevention Committee of the Gynecologic Oncology Group for five years.

He was also president of the Society of Gynecologic Oncology from 2013 to 2014 and president of the International Gynecologic Cancer Society from 2014 to 2016.

Denis Guttridge named director of MUSC Darby Children's Research Institute, associate director at Hollings



Denis Guttridge will join the Medical University of South Carolina as director of the Charles P. Darby Children's Research Institute and associate director of translational sciences for the Hollings Cancer Center effective May 1.

Guttridge most recently served as professor of cancer biology and genetics at Ohio State Comprehensive Cancer Center, where he has worked for the past 16 years. There he served as the associate director for basic research and was responsible for the coordination of basic science across the center's research programs.

His job involved fostering and nurturing collaborations at Ohio State and Nationwide Children's Hospital, involving more than 300 cancer researchers and their teams from 12 of the university's colleges.

The Darby Children's Research Institute, which opened in February 2005,

is the largest and most comprehensive pediatric research facility in the Carolinas and one of only about 20 in the country.

The seven-story, 121,000 square-foot building houses 150 laboratories with 11 research programs dedicated to discovering the cures for a wide spectrum of conditions affecting kids, including cancer, genetic disorders, and diabetes.

Guttridge's research focuses on both early muscle development and cancer. At OSU, he was the principal investigator for multiple NIH research project grants and an NIH research training grant.

A special area of his research focus is the nuclear factor kappa B family of transcription factors and their role in regulating skeletal muscle differentiation. This research made connections that led to insights in a number of disease conditions where NF- κ B activity is chronically elevated.

Guttridge is a scientific leader in the molecular mechanisms of muscle-wasting conditions, including the cancer syndrome called cachexia that is commonly diagnosed in cancer patients and contributes to poor prognosis and a reduced quality of life.

Other research interests include pancreatic cancer that has the highest incidence of cachexia, and childhood illnesses related to skeletal muscle defects including Duchenne muscular dystrophy and a childhood cancer called rhabdomyosarcoma.

In addition to his role in the cancer center at Ohio State University as associate director of basic science, he directed the Center for Muscle Health and Neuromuscular Disorders and led working groups in cancer cachexia and pancreas disease.

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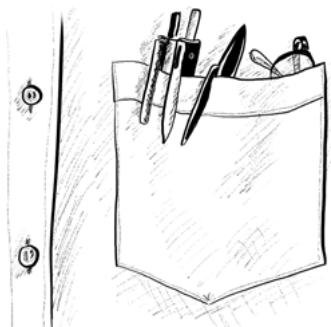
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THE CLINICAL CANCER LETTER



TRIALS & TRIBULATIONS

Diversity within Diversity: Lessons from the Latinos of South Texas



Amelie Ramirez, Dr.P.H.,

Professor and interim chair in the Department of Epidemiology & Biostatistics and associate director of cancer prevention and health disparities at the Mays Cancer Center, the newly named center at UT Health San Antonio MD Anderson Cancer Center



Ruben A. Mesa, M.D.,

Director of the Mays Cancer Center, the newly named center at UT Health San Antonio MD Anderson Cancer Center

Diversity is to be celebrated in our society as enriching our experiences, our cultures and the richness of our lives. Diversity within the context of cancer care and research has appropriately grown to include considerations of diversity of race, ethnic heritage, age, gender, and experiences.

Within the diversity of ethnic heritage, we have learned that deep diversity exists within several additional factors including race, culture, and regional factors. In the context of cancer care and research, these aspects of diversity may impact biological differences between populations, such as cancer incidence and prevalence, predispos-

ing factors, presence of comorbidities impacting therapy, pharmacogenomic differences in cancer therapy metabolism, and even perhaps mutation profiling. Additional cultural differences impact preconceptions of patients regarding medical care, participation in clinical trials, and end-of-life care.

Our cancer center, the Mays Cancer Center at UT Health San Antonio MD Anderson, has the privilege of caring for a predominately Latino population within our catchment area of San Antonio and South Texas.

[See related story on [page 13](#) in *The Cancer Letter*.]

Diversity within Latino Populations

In the late 1980s, most health research focused on “white, black, or other.”

Amelie Ramirez, a researcher at The University of Texas Health Science Center at San Antonio, now called UT Health San Antonio, and its Mays Cancer Center, was among the first researchers to focus on Latino health issues. She and her team developed interventions to address some of the major cancer concerns facing this population.

In the 1990s, her team launched the first comprehensive assessment of a large Latino cohort to identify similarities and differences in knowledge, attitudes, and behaviors for cancer screening and cancer risk factors among different Latinos populations—Mexican Americans in San Diego, San Antonio, and Brownsville, Texas; Cuban Americans in Miami; Puerto Ricans in New York City; and Central and South Americans in San Francisco—where social determinants, acculturation, and ancestry all play a major role in cancer health care outcomes.

The project eventually transitioned into the Redes En Acción network, which has stimulated collaborative research including culturally competent patient navigation to expedite care for Latinas who have had an abnormal mammogram. The network has a program that communicates health messages to Latinos to reduce cancer and has a pipeline to train future researchers.

Today, Latinos account for 18 percent of the nation’s population. But this population remains very diverse. Mexican-origin Latinos accounted for 63.3 percent of the nation’s Latino population in 2015 and were the largest share of any origin group, but that number declined from 65.7 percent in 2008, according to Pew Research Center data. The non-Mexican-origin group has risen from 34.3 percent in 2008 to 36.7 percent to 2015. Puerto Rican-origin Latinos are the second-largest group after Mexican-origin Latinos. Five other Latino-origin groups have populations of more than 1 million—Salvadorans, Cubans, Dominicans, Guatemalans, and Colombians.

Cancer-Specific Issues of Latinos of South Texas

In our South Texas region, more than two of three people are Latino. Only one in three people in the rest of Texas are Latino. Most Latinos in the region are of Mexican origin. This population tends to struggle with lower educational levels, lower per-capita income, and less access to health care compared to the rest of Texas and the nation.

U.S. Latinos deal with many cancer health disparities compared to their white peers, including higher rates of cervical, gallbladder, and liver cancers, as well as acute lymphocytic leukemia. These disparities are even more pronounced in South Texas.

For example:

- Cervical cancer incidence was higher among women in South Texas (10.5 cases per 100,000 women) than in the rest of Texas (9.3/100,000)
- Latina women in South Texas had a higher incidence of breast cancer (95.6/100,000) than Latinas in the rest of Texas (90.7/100,000)

- Liver cancer incidence in South Texas (12.2 cases per 100,000 population) was higher than the rest of Texas (8.4/100,000) and nationally (7.3/100,000)
- South Texas had a slightly higher incidence of stomach cancer (8.3/100,000) than the rest of Texas (6.7/100,000), a rate that was even higher among Latinos in South Texas (11.4/100,000) compared to non-Latino whites (4.7/100,000).

Reducing Latino Cancer Disparities

Guided by this knowledge, Ramirez and other researchers at the Mays Cancer Center are working to reduce cancer health disparities in South Texas from primary prevention all the way to cancer survivorship. The Mays Cancer Center is taking steps to increase Latino accrual into clinical trials, given that fewer Latinos than other population groups participate.

UT Health San Antonio researchers also identified aflatoxins—cancer-causing chemicals produced by mold that can contaminate improperly stored foods, and are ingested by people—as a culprit for the sky-high levels of liver cancer in South Texas Latinos.

Ramirez and her team implemented a cooking and motivational interviewing intervention to help local breast cancer survivors increase their intake of anti-inflammatory foods to fight recurrence.

They built an advocacy education program, Salud America!, to enable people to push for healthy system changes in local communities and schools to improve Latino child and family health. They created a bilingual quit-smoking service for South Texas Latinos called Quitxt, which sends text messages with culturally and regionally relevant sup-

port, and is scientifically proven to help young adults quit for good.

The team is developing smartphone apps to help local breast cancer patients stick to their prescribed therapy. And even more significant, the team is building a pipeline of Latino cancer researchers to continue this important work and innovate new research to improve Latino health.

UT Health San Antonio and its Mays Cancer Center are hosting an international conference, *Advancing the Science of Cancer in Latinos*, to address cancer among the largest majority-minority population in the U.S. More than 200 health researchers, professionals, and leaders are set to attend the conference on Feb. 21-23, 2018, and generate recommendations for future directions of cancer in Latinos.

Individualizing Cancer Care

The revolution of individualized cancer care has deeply swept into cancer centers, and although it began as a way to incorporate tumor-specific mutation analysis informing targeted therapy, it continues to evolve.

Indeed, individualized cancer care now begins with an assessment of mutation profile, possibly adds pharmacogenomic information, is refined by patient input—both verbal and through validated patient reported outcome questionnaires—and finally factors in cultural and ethnic factors that influence cancer diagnosis, treatment, and survivorship.

CLINICAL ROUNDUP



NEJM publishes Loxo's larotrectinib clinical data

The New England Journal of Medicine Feb. 22 published data for larotrectinib in the treatment of pediatric and adult patients whose tumors harbor tropomyosin receptor kinase gene fusions. Loxo Oncology Inc. and Bayer AG are developing the agent

The paper provides additional clinical details and patient follow-up from the 2017 American Society of Clinical Oncology Annual Meeting presentation. It includes the first 55 consecutively enrolled adult and pediatric patients with TRK fusion cancers treated across Loxo Oncology's phase I adult trial, phase II trial (NAVIGATE), and phase I/II pediatric trial (SCOUT), using a July 17, 2017 data cutoff.

"Ongoing treatment with larotrectinib continues to demonstrate striking and durable efficacy coupled with minimal side effects, across a diverse patient population," said David Hyman, the NAVIGATE global principal investigator, chief of the Early Drug Development service at Memorial Sloan Kettering Cancer Center and senior au-

thor of the NEJM paper. "The efficacy of larotrectinib warrants screening for TRK fusions alongside other actionable targets in patients of all ages with advanced solid tumors

In December, Loxo Oncology initiated submission of a rolling New Drug Application to FDA for larotrectinib, utilizing the same patient population and data cutoff as outlined in the NEJM paper. The rolling NDA submission is expected to be complete in early 2018 and a Marketing Authorisation Application submission by Bayer in the European Union is expected in 2018. The larotrectinib program has continued to enroll and treat newly identified patients with TRK fusion cancers, beyond the 55 patients described in the publication.

The anti-tumor activity and safety of larotrectinib in these additional patients are consistent with the data reported in the publication, and will be included for supportive analyses in the NDA and MAA submissions. Loxo Oncology expects to present these additional data in the second half of 2018.

The published data were based on the intent to treat principle, using the first 55 TRK fusion patients with RECIST-evaluable disease enrolled to the three clinical trials, regardless of prior therapy or tumor tissue diagnostic method. The analysis included both adult and pediatric patients, ranging in age from four months to 76 years, who carried 17 unique TRK fusion-positive tumor diagnoses. Tumor types included salivary gland, infantile fibrosarcoma, thyroid, colon, lung, melanoma, gastrointestinal stromal tumor, and other cancers.

The primary endpoint for the analysis was overall response rate. Secondary endpoints included duration of response, progression-free survival, and safety. As shown below, as previously reported, the ORR was 75% by central assessment and 80% by investigator assessment.

Median duration of response and median progression-free survival had not been reached after median follow-up durations of 8.3 months and 9.9, respectively. At 1 year, 71% of responses were ongoing. As of the July 17, 2017 data cutoff, 86% of responding patients remained on treatment or had undergone surgery with curative intent. The first patient treated with a TRK fusion tumor remained in response and on therapy at 27 months.

Larotrectinib was well tolerated with the majority of all adverse events being grade 1 or 2. Few grade 3 or 4 adverse events, regardless of attribution, were observed, with the most common being anemia (11%), alanine or aspartate aminotransferase increase (7%), weight increase (7%), and neutrophil count decrease (7%) (all grade 3 events). There were no treatment-related grade 4 or 5 events, and no treatment-related grade 3 adverse events occurred in more than 5% of patients. Eight patients required larotrectinib dose reductions.

Adverse events leading to dose reductions included AST/ALT elevation, dizziness, and neutrophil count decrease, all grade 2 or 3 events. In all cases, patients whose doses were reduced maintained their best response at the lower dose and none discontinued larotrectinib due to an adverse event.

Primary resistance was observed in six patients in the study. Of the six, one patient had been previously treated with another TRK inhibitor and tumor sequencing prior to larotrectinib dosing revealed a solvent front mutation, a known resistance mechanism. Tumor tissue was analyzed for three of the five remaining patients. In all three patients, TRK immunohistochemistry failed to demonstrate TRK expression, potentially implicating a false positive initial TRK fusion test result and therefore explaining the lack of response in these patients.

The publication also details mechanisms of acquired resistance to larotrectinib. Ten patients experienced disease progression while on treatment after a documented objective response or stable disease for at least six months, a phenomenon known as acquired resistance.

Nine of the ten patients had assessments of post-progression tumor or plasma samples, and NTRK kinase domain mutations were identified in all of those samples tested. In seven of those assessed, investigators identified solvent front mutations as a convergent mechanism of acquired resistance; other NTRK kinase domain mutations were identified in the remaining two patients tested. Of the 10 patients who developed acquired resistance, 80% continued treatment with larotrectinib beyond progression due to ongoing clinical benefit.

DRUGS & TARGETS



FDA expands approval of Imfinzi to reduce the risk of NSCLC progressing

The FDA has approved Imfinzi (durvalumab) for the treatment of patients with stage III non-small cell lung cancer whose tumors are not able to be surgically removed and whose cancer has not progressed after treatment with chemotherapy and radiation.

Imfinzi is sponsored by AstraZeneca.

Imfinzi targets the PD-1/PD-L1 pathways. By blocking these interactions, Imfinzi may help the body's immune system attack cancer cells. Imfinzi was previously granted accelerated approval in 2017 for the treatment of certain patients with locally advanced or metastatic bladder cancer.

The approval of Imfinzi for the treatment of stage III, unresectable NSCLC was based on a randomized trial of 713 patients whose cancer had not progressed after completing chemotherapy and radiation.

The trial measured the length of time the tumors did not have significant growth after starting treatment with Imfinzi or a placebo (progression-free survival). The median progression-free survival for patients taking Imfinzi was 16.8 months compared to 5.6 months for patients receiving a placebo.

In addition, the sponsor has agreed to a post-marketing commitment to provide additional information from their study to the FDA about how long patients lived following treatment with Imfinzi after chemotherapy and radiation (overall survival).

Common side effects of Imfinzi in patients with stage III unresectable NSCLC include cough, fatigue, inflammation in the lungs (pneumonitis/radiation pneumonitis), upper respiratory tract infections, difficulty breathing (dyspnea) and rash.

Serious risks of Imfinzi include immune-mediated side effects, where the body's immune system attacks

healthy cells or organs, such as the lungs, liver, colon, hormone-producing glands, and kidneys.

Other serious side effects of Imfinzi include infection and infusion-related reactions. Imfinzi can cause harm to a developing fetus; women should be advised of the potential risk to the fetus and to use effective contraception.

NCI PROTOCOLS



NCI Trials for February

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 - 10114

Phase I Trial of 5-Aza-4'-Thio-2'-Deoxycytidine (Aza-TdC) in Patients with Advanced Solid Tumors

National Cancer Institute Developmental Therapeutics Clinic
Doroshov, James H.
(240) 781-3320

Phase I/II - ADVL1614

A Phase 1/2 Study of VX15/2503 (IND#136181) in Children, Adolescents, or Young Adults with Recurrent or Relapsed Solid Tumors

COG Phase 1 Consortium
Greengard, Emily G.
(612) 626-2378

Phase I/II - EA9152

A Phase IB/II Study of Venetoclax (ABT-199) in Combination with Liposomal Vincristine in Patients with Relapsed or Refractory T-Cell or B-Cell Acute Lymphoblastic Leukemia

ECOG-ACRIN Cancer Research Group
Palmisiano, Neil David
(215) 503-0432

Phase II - 10100

A Randomized, Phase 2 Trial to Evaluate the Safety and Efficacy of Eribulin Mesylate in Combination with Atezolizumab Compared to Atezolizumab Alone in Subjects with Locally Advanced or Metastatic Transitional Cell Urothelial Cancer Where Platinum-Based Treatment is Not an Option

City of Hope Comprehensive Cancer Center LAO
Quinn, David Ian
(323) 865-3956

Phase II - 10104

A Randomized Phase 2 Study of Cabozantinib in Combination with Nivolumab in Advanced, Recurrent Metastatic Endometrial Cancer

University Health Network Princess Margaret Cancer Center LAO
Lheureux, Stephanie
(416) 946-4501 X 2415

Phase II - A091605

A Randomized Phase II Study of Anti-PD1 Antibody [MK-3475 (Pembrolizumab)] Alone Versus Anti-PD1 Antibody Plus Stereotactic Body Radiation Therapy in Advanced Merkel Cell Carcinoma

Alliance for Clinical Trials in Oncology
Luke, Jason John
(617) 632-6588

Phase II - AMC-103

A Phase 2 Evaluation of VGX-3100, a Synthetic DNA Immunotherapy Targeting Human Papillomavirus 16 and 18 E6 and E7 Proteins, for Anal High-Grade Squamous Intraepithelial Lesions (HSIL) in HIV-Positive Individuals

AIDS Malignancy Consortium
Wang, Chia-Ching (Jackie)
(415) 476-4082 X 146

Phase II - EA3163

Phase II Randomized Trial of Neo-Adjuvant Chemotherapy Followed by Surgery and Post-Operative Radiation Versus Surgery and Post-Operative Radiation for Organ Preservation of T3 and T4a Nasal and Paranasal Sinus Squamous Cell Carcinoma (NPNSCC)

ECOG-ACRIN Cancer Research Group
Saba, Nabil F.
(404) 778-1900

Phase II - EAE161

Perfusion CT to Predict Progression-Free Survival and Response Rate in Bevacizumab and Paclitaxel Treatment of Platinum-Resistant Persistent or Recurrent Epithelial Ovarian, Fallopian Tube, or Peritoneal Carcinoma

ECOG-ACRIN Cancer Research Group
Lee, Susanna I.
(617) 643-2009

Phase II - S1400K

A Phase II Study of ABBV-399 (Process II) in Patients with C-Met Positive Stage IV or Recurrent Squamous Cell Lung Cancer (LUNG-MAP SUB-STUDY)

SWOG

Waqar, Saiama Naheed
(314) 362-5737

Phase II - S1702

A Phase II Study of Isatuximab (SAR650984) for Patients with Previously Treated AL Amyloidosis

SWOG

Scott, Emma Catherine
(503) 494-2398

Phase Other - AALL17B2-Q

Predicting Relapse Based on Deep Single-Cell Phenotyping at Diagnosis

Children's Oncology Group
Davis, Kara Lynn
(650) 724-8073

Phase Other - ARST17B2-Q

Germline Genetic Landscape of Pediatric Rhabdomyosarcoma

Children's Oncology Group
Lupo, Philip
(713) 798-2960

NCI Community Oncology Research Program (NCORP) clinical trials:

Phase Other - EAQ162CD

Longitudinal Assessment of Financial Burden in Patients with Colon or Rectal Cancer Treated with Curative Intent

ECOG-ACRIN Cancer Research Group
Kircher, Sheetal Mehta
(312) 695-6180

Phase Other - WF-20817CD

Implementation of Smoking Cessation Services within NCI NCORP Community Sites with Organized Lung Cancer Screening Programs

Wake Forest NCORP Research Base
Foley, Kristie L.
(336) 713-5084

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