

A Conversation with NCI Acting Director, Dr. Douglas R. Lowy
Precision Medicine and the NCI Budget
June 1, 2015

Operator

Welcome and thank you for standing by. All participants will be on a listen only mode until the question and answer session of today's call. At that time you can press *1 to ask a question from the phone lines. I'd also like to inform parties that this call is being recorded, if you have any objections, you may disconnect at this time. And I'll now turn the meeting over to Ms. Kelley Landy. Thank you ma'am, you may begin.

Kelley Landy – Acting Director, Office of Advocacy Relations – National Cancer Institute

Hi everyone, thank you all so much for taking time to join us today. I'm Kelley Landy, the Acting Director of the Office of Advocacy Relations here at the National Cancer Institute. Thanks again and a special thank you to all of our colleagues who have taken time out of their busy ASCO schedules to tune in. As you all know, today we have Dr. Doug Lowy, Acting Director of the National Cancer Institute here with us. Dr. Lowy is here today to discuss research priorities including the Precision Medicine Initiative and its potential to lead to better treatment through predictive oncology. In addition, Dr. Lowy will be discussing the challenging budget environment facing NIH and NCI.

Just to all of you, we know that you all have summer and fall activities planned, a note about your efforts; as an Institute we are very appreciative of the passionate commitment you all bring to cancer research. Your voice and perspectives are critical to getting the best treatments to patients and we really value these interactions with you. We view this as a series of discussions throughout the coming year.

After Dr. Lowy's presentation there will be some time for questions. So we have received a few questions ahead of time and we'll answer those first; as time permits we'll be taking a few of your questions live as well. Please do use the chat function for your questions and send those over in advance, just to save time so we can hear from as many of you as possible. So now I'm going to pass the webinar over to Dr. Lowy so we can hear more about NCI's priorities and hear from all of you. Thank you.

Douglas Lowy, MD - Acting Director - National Cancer Institute

Thanks very much, Kelley. Good afternoon and good morning to those of you who are on the West Coast and on Mountain Time. It's a pleasure for me to have this opportunity to talk with you about some aspects of what's going on at NCI and as Kelley mentions, I'm going to be emphasizing two particular areas; one is precision medicine, especially as it is related to cancer treatment and the other is some current budgetary issues. We are very grateful for those of you who are on the phone and also for your efforts to try to support the NCI in various ways.

The first issue that I wanted to cover today is, "What is Precision Medicine?" There's been a lot of buzz about it and I think that many people aren't entirely clear about what it might be. So the area of precision medicine or personalized medicine got a real stimulus back in 2011 with the

publication of this report called “Towards Precision Medicine,” which was published by the National Research Council. And this signature figure from the report emphasizes first that it was a taxonomy which really has to do with understanding what the molecular pathology is and the pathogenesis of disease. And then the precision medicine talking about how it makes for an accurate diagnosis, targeted treatment and improved health outcomes.

This was an excellent and important--this was an important publication and what it said, as shown here in this box is that precision medicine or personalized medicine refers to the tailoring of medical treatment to the individual characteristics of each patient. Preventive or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not. I think that this definition is very good for treatment; however, it inadvertently appears to exclude population-wide public health recommendations, even those based on mechanistic understanding of disease.

And so I have made a somewhat amended version where the first sentence is that it's interventions to prevent, diagnose or treat a disease based on molecular or mechanistic understanding of the causes, pathogenesis or pathology of disease. But as said in the precision medicine report, where the individual characteristics of a patient are sufficiently distinct, interventions can be concentrated on those who will benefit, sparing expense and side effects for those who will not.

Before we leave this, I just wanted to point out that precision medicine is being used, for example now in cervical cancer screening, where understanding that virtually all cases of cervical cancer are caused by HPV infection. We are in the process of really being in the transition from Pap smear or cytology-based screening to HPV-based screening because several studies have shown that HPV-based screening can be even more effective in reducing the incidence of cervical cancer than Pap smear screening.

But let's go on to precision medicine trials to improve patient outcomes, which were therapeutic trials and there are several that have been begun since the beginning of last year. Slide number 7 shows you a list of four different trials that were initiated since the beginning of last year; one is the Lung-MAP trial, which is a trial of lung squamous cell cancer. It is a master protocol in the sense that it is testing a number of different molecular abnormalities and a number of different targeted treatments. There's also the ALCHEMIST trial, the Adjuvant Lung Adenocarcinoma Enrichment and Sequencing Trial, the MPACT trial and the Exceptional Responders Trial. All of these trials are different versions of trying to match the targeted treatment to the particular molecular abnormality in the patients that are in the trial with the outcome hoping to be that there will be improved responses as a result of the targeted treatment.

Turning to slide number 8, which is--talks about the NCI-MATCH Trial, which is the trial that has been announced today at ASCO. It has been in the works for a long time. It is the largest and most rigorous precision oncology trial and its goal is for the foundation discovery that focuses on molecular abnormalities rather than on the site of tumor origin. And it uses a validated and standardized gene sequencing and selection targeted therapy that is--we refer to as the matchbox for developing the--treatments for individual patients. The trial was co-developed

by NCI and by ECOG-ACRIN as part of the National Cancer Trials Network and it is going to be available virtually any place in the United States with more than 2400 sites nationwide.

The adult MATCH trial changes the current clinical paradigm to a new paradigm, as shown in slide 9. The current paradigm is to evaluate drugs in a particular cancer type at a particular organ site, whereas the MATCH trial follows a paradigm that's based on targeted treatment of specific, actionable molecular abnormalities in cancer independent of the organ site. Actionable means that there either is an FDA- approved targeted drug for that abnormality or there is an investigational drug that targets that abnormality. And the trial is a public private partnership with about 20 different pharmaceutical companies at the moment testing a range of targeted treatments in a single trial. It will test either off-labeled use of FDA-approved drugs or investigational drugs. By bringing together this large number of companies and large number of targeted treatments, it is much more likely that a patient who is interested in entering this trial there will be a drug available for him or her as a result of the screening.

The pediatric MATCH trial is currently under discussion. It's for children with advanced cancers that have progressed on standard therapy, but it is modeled after the adult MATCH trial where DNA sequencing will be used to identify children whose tumors have a genetic abnormality for which there is either an approved or an investigational targeted drug. And it's a partnership of--with the NCI-funded Children's Oncology Group, but it's still, as I mentioned under development but a timetable for launch or patient enrollment will be available soon.

I'd now like to turn more specifically to the Precision Medicine Initiative to define what it is and how we are trying to take advantage of precision medicine in ways beyond the clinical trials. Precis--this is part of President Obama's FY-16 budget proposal that would start in October of this year. And the President's proposal has four parts; the part that we'll be focusing on is the expansion of the application of precision medicine in cancer treatment, but you should also be aware that there is a component to establish a cohort of 1 million or more volunteers to help bring precision medicine to a wide range of diseases. An increase in the FDA's capacity to support the advance of precision medicine in regulatory issues and to develop interoperability standards for data exchange across systems while protecting privacy that is for the Office of the National Coordinator for Health Information Technology.

In precision oncology, The Cancer Genome Atlas or TCGA allies a large number of tumors from a different type of tumor types and is in the process of being completion, but as a consequence, we have a much greater appreciation of and understanding of the complexity and the molecular abnormalities in cancer. And we have initiated a number of different trials, most of which I had discussed in a previous slide. In addition, as just mentioned, there is the NCI-MATCH trial which has just been approved and launched and it will be having the characteristics that I mentioned.

But what we're hoping to have happen as a result of the president's initiative is what we are calling NCI-MATCH Plus, which is scaling of the NCI Precision Medicine Initiative to leverage the critical mass from previous genomic research to broaden molecular profiling in NCI-supported trials, use early signals to direct new trials. And the potential, it has the potential to

change cancer clinical trial paradigms, as I had mentioned and to discover new mechanisms of reaction or resistance to novel therapy and in addition, to try to overcome that resistance.

So what is in the 70 million dollar proposal requested by President Obama to expand the genomics-based clinical and pre-clinical studies? First, as mentioned, it is the MATCH trial of adult and pediatric cancer, but in addition there will be a repository of patient derived pre-clinical models for evaluating targeted therapy and importantly, to try to understand drug resistance and to overcome it, especially with the promise and the potential of combination treatment. And in addition, there will be a National Cancer Database to integrate genomic information with clinical response and outcome.

So I now turn to the last topic, which really is the NCI budget of 2015 and 2016 and how it works. This diagram shows for you first that ongoing and long-term projects, infrastructure and training programs make up more than 80% of the annual budget and therefore, as shown in the bottom right, each year only a small portion of the budget is actually available for new projects. And the new projects are divided between a number of different components which include basic research, translational research, clinical research and supporting the cancer research infrastructure.

And these projects in addition, the basic science as shown on the next slide, really forms the baseline for the breakthroughs and new initiatives that are going to give us even better outcomes we hope, with cancer in the future. Just under one-half of NCI's budget supports basic research. But as depicted here, this then leads to improvements in prevention, detection, diagnosis and treatment with the goal of fewer people getting cancer and those who do develop cancer, to live longer lives thanks to the investment in basic science.

What about the NCI budget itself? This slide shows you what the budget has been like between 1998 and currently. And what I hope you can appreciate, on the left side of this is the so-called doubling of the budget where between 1998 and 2004, the budget for the NCI just about doubled, as shown in the blue, the light blue bars. The dark blue or dark green bars actually show you however, what has happened to the purchasing power of that money. And you can appreciate, I think, how the purchasing power for the NCI budget has gone down substantially over the last 10 years so that we have, now have at our disposal in terms of purchasing power, we're just about back, as shown in this horizontal dotted line, where we were in 1999 after the first year of the doubling.

What has been the impact of this on the success rate for grant applications for basic translational applied research, etcetera? This next slide shows you what has happened with funding mechanism--with the funding success rate since the late 1970s up until--through last year and what I hope you can see is that prior to the doubling of the budget that success rates generally were between 25% and 35%, which means that between 1 and 4 and 1 in 3 applications were actually funded. Starting with the end of the doubling of the budget, as shown here with the green--with the horizontal green bar around 2004, there has been a continuing and rather marked drop in the success in the funding rates so that now it's closer to about 15% success, which translates

essentially to 1 in 6 or 1 in 7 applications are actually successful. So, there are many meritorious applications which we simply are not able to fund.

So the President's FY-16 budget appropriation is for a 1 billion dollar increase for NIH as a whole, essentially to go from just over 30 billion dollars in the FY-15 appropriation to just over 31 billion dollars. And within that increase has been proposed a 145 million dollar increase for NCI to go from just about 4.95 billion dollars to essentially 5.1 billion dollars so that we would be back up above 5 billion dollars, which is where we were several years ago.

So let me try to summarize that what I've tried to tell you is first that precision medicine represents a rational approach to cancer prevention and screening that we hope will lead to further decreases in the incidence of cancer and further improvement in the outlook for patients who develop cancer. The Precision Medicine Initiative will enable the field of predictive oncology and the goal of that field is to deliver the right drugs to the right patient. Thank you very much for your attention and I'll be happy to try to address some questions and comments.

So one question that we have received is, what is NCI's greatest research challenge in the near-term? And the greatest challenge I think by far is deciding which of the many meritorious uses of the money we are going to choose to fund. And on some level as a consequence, choose not to fund. We would be in a much stronger position if we were able to fund a higher proportion of the meritorious activities that are proposed to us.

Kelley Landy

And I think we have one more submitted question about targeted therapies on specific pathways if you would address.

Doug Lowy, MD

So this question says targeted therapy directed towards specific pathways seems especially challenging in cancers which contain several genomic signatures within a tumor. How can this be overcome considering the great expense of each targeting agent? And I think the simple answer would be, through our doing more research so that we can understand when there are multiple pathways, which pathways tend to predominate and particularly the notion of using combination treatment to interfere with more than one of those pathways. The precise combination, however, is going to depend on the cancer in question and that's why I think that precision medicine in the long term what really is going to help patients more than anything else is developing a clear understanding of predictive oncology so we will be able to predict what kind of treatment each patient should be receiving.

Kelley Landy

Okay, at this time I'm going to move over to the live chat to check and see what live questions we received during this webinar; so if you all will bear with us for just a second.

Doug Lowy, MD

I understand that one of the questions is whether the NCI will be having future initiatives that will be focused on primary prevention of cancer? And the--and I think that I can say that we are

certainly very interested in trying to identify causes of cancer and understand how those causes bring about cancer. And thereby using that understanding to try to intervene to prevent cancer, usually either through exposure of the causative agent or through the development of interventions that reduce the seriousness of the exposure.

A classic situation is the development of vaccines against viruses that cause cancer. And one of the areas of considerable interest is the area of Epstein-Barr virus infection which causes a variety of cancers and most recently it has been linked to a proportion of stomach cancers, but in addition, Burkitt lymphoma, non-Hodgkin's lymphoma and nasopharyngeal carcinoma. And so there is considerable interest in trying to develop a vaccine against that, as well as other classic interventions that really have to do with reducing exposure. Thank you.

Kelley Landy

Great. So another question that we just received Doug, if you don't mind weighing in is, with immuno-oncology looking so promising right now, what are the plans for incorporating studies of the individual immuno--into precision medicine therapy, treatment and trial design?

Doug Lowy, MD

Thank you for that question. The question correctly identifies this as a potentially important area and we see this in the context of the precision medicine trials, particularly with the opportunity for combination treatment. We hope that understanding the basis of resistance that this will contribute importantly towards overcoming that area. Thank you.

Kelley Landy

Great. So we're just looking at a few more questions coming in and there's a question here on CMS policy and coverage, Doug, if there's any comment you can make on the top here. It's is NCI doing anything to align research priorities for precision medicine with CMS policy and coverage?

Doug Lowy, MD

I would say that we help to contribute to the science that leads to the coverage and that's the principal way in which we end up aligning with CMS. But we are by nature, we tend to be doing studies that are off-label for FDA approved drugs or that are looking at investigational drugs whereas CMS is really focused on standard of care. We generally use standard of care as our baseline.

Kelley Landy

Okay, it looks like we have one additional question here that Doug will address and this will have to be Doug's last answer and--or question and please feel free to follow up with the Advocacy Office, I'll give you our e-mail at the end.

Doug Lowy, MD

Yes, the question really is how advocates can help until the trial opens in July? And I think that if you interact with Kelley and others in the Advocacy Office, they can really give you assistance in this area. We are delighted that you are excited about this. We think that this trial has the

potential to really advance cancer research substantially and its flexibility. One of the things we really like about it is that if new drugs come online, it's possible to incorporate them with a relatively short lead-time into the ongoing trial. So it has really a lot of flexibility built into it and we hope that it will lead to identifying interventions that work very well and can be--lead to approval in a shorter timeframe than usual.

Kelley Landy

Great. Thank you Doug very much. Thanks very much for joining us today; we appreciated hearing from Dr. Lowy and we appreciated all of the questions you all had today. Please do follow up with the Office of Advocacy Relations so we can continue this dialogue. You can reach us at NCIadvocacy@nih.gov and we want to thank you all again for your time and for your participation and especially thank Doug for attending today and speaking with all of us. So that concludes the webinar and we hope to hear from all of you soon.

Operator

Thank you that does conclude today's conference. Thank you all for participating, you may disconnect your lines at this time.