89th Meeting of the National Cancer Institute (NCI)
Council of Research Advocates (NCRA)
National Institutes of Health (NIH)

Virtual Meeting
June 21, 2023

Members Present

Mr. Yelak Biru
Dr. Victoria Buenger
Mr. Marty Chakoian
Ms. Annie Ellis, *Chair*
Mr. Nathaniel Ferre
Ms. Joya Delgado Harris
Dr. Brittany McKelvey
Mr. Robert Riter
Ms. Kristen Santiago
Mr. Kevin Stemberger
Dr. Nicole Willmarth

Speakers

Ms. Holly Gibbons, Deputy Director, Office of Government and Congressional Relations, NCI
Dr. Douglas Lowy, Principal Deputy Director, NCI
Dr. Sheila Prindiville, Director, Coordinating Center for Clinical Trials, NCI
Dr. Meredith Shiels, Senior Investigator, Division of Cancer Epidemiology and Genetics, NCI
Ms. Amy Williams, Director, Office of Advocacy Relations (OAR); Executive Secretary, NCRA, NCI

Contents

Welcome and Opening Remarks

Ms. Amy Williams and Ms. Annie Ellis

Ms. Williams opened the meeting at 12:01 p.m., welcomed Council members and attendees, provided brief opening remarks, and reviewed the day's agenda.

Ms. Ellis called the meeting to order, reviewed the conflict-of-interest rules, read the public comment statement, and confirmed that a quorum of members was present.

NCI Principal Deputy Director's Update

Dr. Douglas Lowy

Dr. Lowy provided an overview of the debt ceiling agreement and NCI budget, cancer drug shortages, and research initiatives and advances.

- Dr. Lowy began by summarizing the U.S. debt ceiling agreement that was reached in the beginning of June 2023 and will likely affect funding for many government agencies, including NIH.
- Dr. Lowy then provided an overview of NCI's budget over a 20-year period (2003-2023) and the President's NCI budget proposal for Fiscal Year (FY) 2024, which includes a $500 million increase. He highlighted that this and other proposed budget increases may be in jeopardy due to the debt ceiling agreement.
- Dr. Lowy outlined the Cancer Moonshot's goals and spoke about Dr. Shiels's study, which concluded that cancer death rates must decline faster to achieve those goals.
- Dr. Lowy emphasized the negative impact that the recurring shortages of oncology agents are having on cancer research and patient care, especially pediatric patients. Currently, there are 170 studies with shortage list oncology agents on their protocol. This shortage of cancer drugs is having a larger impact on patients trying to receive standard of care who are not on trials. NIH, the White House, and the FDA are working together to address these shortages.
- Regarding NCI's new initiatives, Dr. Lowy briefly described the Clinical Trials Innovation Unit (CTIU) that will build better, faster, and more accessible cancer trials, the new Combination Therapy Platform Trial with Molecular Analysis for Therapy Choice (ComboMATCH), and the Persistent Poverty Initiative.
- Dr. Lowy shared results from Cancer Therapy Evaluation Program (CTEP) trials presented at the American Society of Clinical Oncology (ASCO) Annual Meeting in 2023, including a trial of nivolumab plus doxorubicin, vinblastine, and dacarbazine (AVD) or brentuximab vedotin plus AVD in patients with newly diagnosed advanced stage classical Hodgkin Lymphoma as well as a study of pre-op chemotherapy with selective chemoradiation versus chemoradiation for patients with locally advanced rectal cancer.
- The Childhood Cancer Data Initiative's (CCDI) accomplishments to date and priorities for the future are discussed in the publication titled *The Childhood Cancer Data Initiative: Using the Power of Data to Learn From and Improve Outcomes for Every Child and Young Adult with Pediatric Cancer*. Dr. Lowy encouraged Council members to read this study.

- A request for information (RFI) has been published to inform future resource allocation and acquisition strategies that can accelerate the development, availability, and evaluation of RNA-based cancer vaccines.
- Dr. Lowy presented results of a phase 3 trial that shows survival benefit of targeted treatment for patients with resected epidermal growth factor receptor (EGFR)-mutated non-small cell lung cancer (NSCLC). This study investigated whether adjuvant osimertinib, which has become standard of care for patients with advanced lung cancer, is useful for patients with less advanced lung cancer (i.e., completely resected, EGFR-mutated, stage IB to IIIA NSCLC).
- Dr. Lowy closed by discussing ideas for the possible role of NCI in increasing access to cancer care and control. He highlighted that NCI does not set health care delivery policy but can work with groups to achieve wider and more equitable dissemination/access to health care delivery, which is an important goal of the Cancer Moonshot.

Discussion

- Ms. Ellis expressed excitement about the Persistent Poverty Initiative. Dr. Lowy shared that 20 years ago there was no difference in cancer outcomes and mortality rates between rural and other areas. Despite advances in cancer treatments and screening and prevention, rural cancer disparities have grown. Dr. Lowy highlighted that since 2016, NCI has focused on rural areas and persistent poverty.
- Ms. Santiago noted that a study showed that racial/ethnic minorities are less likely to undergo biomarker testing, which the LUNGevity Foundation is interested in increasing access to. She asked about NCI convening groups to work on increasing access to cancer care and control. Dr. Lowy clarified that NCI may convene groups that could better explain access issues and how to address these challenges; this initial effort would be small because this is not a traditional approach at NCI. Dr. Lowy added that patient advocacy organizations can be helpful in prioritizing activities.
- Dr. Willmarth shared that in addition to genetic testing, methylation profiling is also critical for brain tumors. She appreciated that NCI is including patient advocacy organizations and the research community in helping prioritize areas as molecular data is collected. Dr. Lowy explained that methylated genes are generally under expressed (i.e., inactivated) and frequently, methylated genes are tumor-suppressor genes.
- Mr. Biru shared that the National Comprehensive Cancer Network (NCCN) is generating social determinants of health (SDOH) screening guidelines and recommendations. He added that during this process, there has been pushback due to policy or legislation not being able to address poverty, ruralness, or overall SDOH. He asked for advice on how to address this pushback. Dr. Lowy noted he would discuss this issue with NCI colleagues and share suggestions.
- Mr. Ferre pointed out that the definition of rurality seems to be primarily dominated by an East Coast perspective and does not involve the Mountain West, West Coast, or Midwest perspectives. Rurality can be defined using landmass or population concentration. Mr. Ferre asked whether NCI plans to provide further guidance for the definition of rurality and whether the differing definitions will be considered a disparity. Dr. Lowy replied he would discuss this issue with Dr. Bertagnolli, who is from Wyoming and has strong connections to that region.
- Ms. Harris asked what NCRA members could do about the ongoing cancer drug shortage.

Dr. Lowy replied that NCRA members could call attention to this problem and pointed out that this issue is persistent and likely requires structural change. Ms. Williams added that NCRA members' unique role of working with several organizations enables them to connect the dots across multiple groups and agencies. She clarified that the day's presentations aimed to inform members about the impact of this drug shortage and that there are no specific requests for the advocacy community.

- Ms. Ellis noted that there are organizations that are involved in addressing the drug shortage. A major oncology medical group has a webpage with actions focused on addressing the drug shortage. Ms. Ellis encouraged members to keep demanding long-term solutions after the current drug shortage is resolved.
- Dr. Buenger commented that there was a large shift in pharmaceutical companies regarding generics; understanding this global change in the industry and drug manufacturing would be informative for policy solutions.
- Mr. Chakoian shared that Black men die of prostate cancer at more than twice the rate of other populations due to health delivery disparities. He asked whether NCI could help eliminate barriers and overcome health disparities. Dr. Lowy clarified that an advantage of the Cancer Moonshot is the implementation of the all-of-government approach. Cancer is predominantly a disease of older people; thus, Medicare has a disproportionate influence and impact on reimbursement. If there are structural issues, the government is poised to improve the situation and CMS can make standard of care recommendations.
- Mr. Biru asked about the Cancer Moonshot goal of reducing cancer mortality by at least 50% in the next 25 years and whether there is urgency to change the rate of cancer death decline from 2.3 to 2.7%. Dr. Lowy replied that it would be best to reach a higher rate of cancer death decline as soon as possible. The Cancer Moonshot goal of ending cancer as we know it requires ensuring that everyone who gets cancer has the possibility of an intervention that will benefit them and making advances in rare cancers and cancers that have not had much progress to date. Examples of potential advances include Kirsten rat sarcoma virus (KRAS) inhibitors being tested in early phase trials for pancreatic cancer and screening/prevention of invasive anal cancer.

Opportunities for Achieving the Cancer Moonshot Goal

Dr. Meredith Shiels

Dr. Shiels presented results of the study titled "Opportunities for Achieving the Cancer Moonshot Goal of a 50% Reduction in Cancer Mortality by 2047" that was recently published in *Cancer Discovery*.

- This project was conducted in response to Dr. Lowy's request for the examination of the feasibility of President Biden's Cancer Moonshot goal of reducing age-standardized cancer mortality rates by at least 50% over the next 25 years.
- Dr. Shiels's analysis estimated cancer incidence, relative survival, and mortality; calculated mortality rate projections from 2022–2047 focusing on the leading 6 causes of cancer death in 2019 (i.e., lung and bronchus, colorectal, pancreas, female breast, prostate, and liver and intrahepatic bile duct [IHBD] cancers); and identified some of the most promising and realistic opportunities to further reduce cancer death rates over the next 25 years. The projections in this study inform whether efforts are on or off track to meet the Cancer Moonshot goal.

- Although not included in this study, less common cancers such as pediatric cancers and exposures are important and should be studied. She also clarified that the study's findings are not recommendations for DCEG or NCI priorities.
- Dr. Shiels presented incidence rates, relative survival, and mortality rates for all cancers (total cancer) noting that over the last few years there has been progress in mortality rate reduction—the rate of decline accelerated during 2016–2019 to 2.3%). She highlighted that to meet the Cancer Moonshot goal, the cancer mortality rate decline must accelerate to 2.7%.
- The approaches to accelerate progress identified are cancer type specific and highlight established interventions with the greatest promise. Regarding modifiable risk factors, except for cigarette smoking, implementation of population-level interventions that reduce risk factors is challenging.
- This study focused on cancer treatments with large survival benefits for a substantial fraction of cancer patients, not on treatments with limited survival benefits that are important but unlikely to have an impact at the population level. Addressing disparities in cancer prevention, early detection, and treatment in many of the opportunities outlined in this study is critical.
- Dr. Shiels presented incidence rates, relative survival, mortality rates, and potential interventions (i.e., prevent incidence or mortality) and opportunities to accelerate progress for each cancer type.
- Regarding lung cancer, there is hope for meeting the Cancer Moonshot goal due to progress in smoking declines from recent years not yet impacting lung cancer death rates, the low number of high school students initiating smoking, and proposal of new tobacco product standards. Disparities in cigarette smoking remain. Because smoking causes many different types of cancer, progress against smoking would have a broad impact. Other opportunities include increasing low-dose computed tomography (CT) uptake and reducing disparities in its use as well as reducing disparities in access to effective treatments (e.g., NSCLC treatments).
- The observed colorectal cancer (CRC) mortality rates indicate that the Cancer Moonshot goal will not be met. All identified opportunities focus on screening (i.e., early detection, prevention). Dr. Shiels described current screening guidelines, mortality reductions of different screening tests, opportunities for enhancement in screening uptake, and the importance of follow-up upon positive results after non-invasive screening.
- Pancreatic cancer incidence and mortality rates continue to increase, and prevention and early detection of pancreatic cancer remain challenging. Opportunities include development and evaluation of new mutant KRAS inhibitors, which may be the greatest promise for increasing survival of a substantial fraction of pancreatic cancer patients.
- Breast cancer incidence and survival has increased; however, the mortality rate trend indicates acceleration of progress is needed. Opportunities include the evaluation of efficacy of low-dose hormone therapies and improvement of risk stratification; evaluation of strategies for increasing physical activity and decreasing obesity in survivors; and increasing mammography, hormone therapy, and chemotherapy uptake, especially in underserved populations.
- Prostate cancer incidence, survival, and mortality rate patterns are complicated: incidence rates for 2014–2019 have increased, whereas survival remains high. After a strong decline, mortality rates flattened out for 2013–2019. Some of the changes in incidence may be due to changes in guidelines for prostate specific antigen (PSA) testing. Opportunities include evaluation of risk-stratified PSA screening and improved diagnostic testing and evaluation of strategies to further reduce overtreatment and disparities.

- Incidence and 3–5-year survival for liver/IHBD cancer have improved since 2015; though survival remains poor. During 2016–2019, the decline of liver/IHBD cancer mortality was not significant, whereas that of liver cancer was only -1.8% per year. Opportunities include increase in uptake of Hepatitis B and C treatments, decrease in smoking prevalence, and increase in cirrhosis diagnosis and screening uptake. Dr. Shields described multiple modifiable risk factors associated with liver cancer deaths and emphasized the disparities in access to direct acting antiviral agents, the benefits of hepatitis treatment, and the importance of screening individuals with cirrhosis.
- Dr. Shiels outlined the next 9 leading causes of cancer death, highlighting that mortality rates for all except brain and other central nervous system and uterine corpus cancers have declined significantly in recent years.
- Limitations of this study include an assumption that recent changes will continue without factoring in exposures, prevention, and treatment; optimistic projections; and deviation between 50% decline in age-adjusted mortality rates and similar decline in the number of cancer deaths due to the aging U.S. population.
- To reach 50% reduction in cancer mortality rates by 2047, accelerated progress and addressing underutilization of known prevention, detection, and treatment strategies and disparities are needed.

Discussion

- Ms. Santiago inquired whether Dr. Shiels considered environmental risk factors (e.g., forest fire smoke, radon) when analyzing progress against lung cancer. Dr. Shiels explained that the study focused on main risk factors (cigarette smoking), which may have a large effect. Environmental risk factors are important for lung cancer but do not have a large population-level effect and may be difficult to quantify.
- Mr. Ferre agreed and suggested future studies should examine radon, for which there are data available. Washington, California, and Utah, which have not eradicated lung cancer, have the lowest rates of smoking and highest rates of radon. Dr. Shiels noted that the NCI Intramural Research Program has a branch that conducts research on occupational and environmental exposures.
- Dr. Willmarth asked what the implications of e-cigarettes may be for lung cancer and whether there is an opportunity for reduction of lung cancer incidence and mortality. Dr. Shiels noted that sufficient e-cigarette product data has not yet been collected to determine implications and opportunities. It is unlikely that e-cigarettes have a similar effect to that of cigarette smoking. Possibly, increased use of noncombustible products is decreasing the use of cigarettes.
- Regarding metastasis, Dr. Willmarth asked whether there are opportunities such as increased screening that may have a significant impact. Dr. Shiels said she will look into this question for the future and added that cancer registries do not collect follow-up or recurrence data, which is a limitation.
- Mr. Chakoian asked whether Dr. Shiels is studying the preventive effects of healthy diet and exercise on various cancers. Dr. Shiels noted that measuring progress at a population level due to physical activity and healthy diet is challenging. These factors are important and, at the individual level, physical activity and healthy diet do affect risk, but no specific interventions were

identified in this study.

- Ms. Ellis expressed appreciation for Dr. Shiels's work and for focusing on reducing both incidence and mortality. She asked whether a follow-up study on uncommon cancers is planned and whether it is possible to show that providing standard of care to areas of persistent poverty could reduce cancer mortality by 50%. Dr. Shiels shared that disparities in cancer care are a topic that is of interest to her and her team. There are profound disparities at every intervention point; thus, increasing access to current effective interventions would have a large impact. One potential approach is identifying the best mortality rates in the country and determining the effect of applying those rates to all areas.

NCI Clinical Trials Innovation Unit

Dr. Sheila Prindiville

Dr. Prindiville presented an overview of NCI's strategic vision for clinical trials and the Clinical Trials Innovation Unit (CTIU).

- Challenges of current cancer clinical trials include high costs, a slow and cumbersome activation process, delayed results, burdensome designs, inequitable access, and excessive data collection.
- To address this current unsustainable clinical trial model, the Clinical Trials and Translational Research Advisory Committee (CTAC) formed the Strategic Planning Working Group in 2020. This working group assessed NCI's strategic vision for clinical trials for 2030 and beyond and developed 15 recommendations and 3 operational initiatives with a broad range of themes.
- NCI's strategic vision for clinical trials is to develop flexible, faster, simpler, less expensive, high-impact clinical trials that seamlessly integrate with clinical practice. Key recommendations are to 1) streamline processes for trial design and execution, 2) focus on essential endpoints, 3) decrease regulatory hurdles and broaden trial access, and 4) increase efficiency of data collection.
- CTIU was formed due to the need to radically transform how clinical trials are conducted by rapidly identifying and testing the most innovative approaches without disrupting ongoing processes, infrastructure, and trials.
- CTIU's aims are to reduce complexity through new models of scientific partnerships and collaborations for innovative science, promote equitable clinical trials participation, and complement the National Cancer Plan and Cancer Moonshot's goals.
- The expertise of NCI, FDA, and the extramural clinical research community are brought together within CTIU to advance clinical care and equitable clinical trials participation for a few high priority studies through innovative science, trial designs, and operational efficiencies.
- NCI's National Clinical Trials Network (NCTN) is a current extramural community partner. CTIU plans to include NCI Community Oncology Research Program (NCORP), industry, and advocacy community partners.
- CTIU plans to develop impactful and transformative therapeutic agents, preventive strategies, imaging, and biological markers, produce high-impact actionable results, streamline trial designs and data collection, and rapidly conduct innovative studies in existing NCI networks.
- Dr. Prindiville provided examples of trials that would be appropriate for CTIU. Innovation is critical and could be achieved via novel interventions, biomarkers, data extraction, or collaborations.

- The Pragmatica-Lung study (S2302) that is led by SWOG Cancer Research Network in collaboration with the Alliance for Clinical Trials in Oncology is an example of an ongoing streamlined clinical trial. Dr. Prindiville highlighted that this trial focused on essential endpoints to reduce the burden on study sites and participants and that this model is not appropriate for all clinical trials.
- Trial evaluation and activation by CTIU involves a 1–2-page submission by investigators followed by rapid vetting and collaborative protocol development with execution in NCI networks.
- The CTIU is in its pilot phase and limited to NCTN; NCTN members and affiliated academics as well as industry proposals with NCTN partners are being reviewed. In later phases, CTIU will likely accept proposal submissions from additional groups. Patient advocates will be involved in the selection process.

Discussion

- Ms. Ellis expressed excitement for the streamlining of clinical trials and asked whether NCORP will be involved in the review process to determine whether these trials are scalable to recruitment at NCORP sites. Dr. Prindiville clarified that several of the NCTN sites are also NCORP sites and NCORP will have input in the review process.
- Mr. Riter asked if this approach is being used to determine whether all clinical trials can become more expedient. Dr. Prindiville indicated that streamlining and innovative activities are being done with a few specific trials but, in the future, some streamlining activities could be incorporated into the clinical trial workstream to generate better trials.
- Ms. Ellis commented on the cost of clinical trial administration emphasizing that designing nimbler trials would be beneficial.
- Ms. Ellis noted that administration is very expensive and improving trials or making them nimbler would be beneficial. Dr. Prindiville noted that CTIU is one of multiple approaches that are being implemented to streamline clinical trials.
- Dr. Willmarth asked whether the use of real-world data would be considered an innovative and appropriate approach by the CTIU. Dr. Prindiville responded that novel approaches for data collection and novel trial designs would be appropriate. The innovation could also be in operational activities that may ultimately have an impact on the whole system. As the CTIU effort progresses, Dr. Prindiville hopes that the types of novel approaches and ideas that are considered will expand.
- Mr. Biru asked how to ensure that clinical trial design remains patient-centric while streamlining data collection (e.g., elimination of some patient-reported outcomes). Dr. Prindiville agreed that the balance between being patient-centric and collecting data is important. Collection of patient-reported outcomes depends on the trial design—in some studies, patient-reported outcomes may be critical.

Legislative and Budget Update

Ms. Holly Gibbons

Ms. Gibbons provided an update on the debt limit deal, the ongoing FY 2024 appropriations process, and recent congressional briefings.

- The debt ceiling agreement recently reached by Congress and the Biden administration raised the debt ceiling until January 2025. This agreement is part of the Fiscal Responsibility Act (FRA), which was signed into law by President Biden on June 3, 2023.
- Ms. Gibbons described how provisions in the debt ceiling agreement may affect NIH, NCI, and other federal agencies. The deal would cap nondefense discretionary spending (source of NIH and NCI funding) for FY 2024 at FY 2023 levels and limit nondefense discretionary spending growth to 1% for FY 2025. If Congress does not pass all 12 appropriations bills by the end of 2023, government spending for FY 2024 would be cut by 1%.
- Following passage of the FRA, 11 Republican Party members derailed House activities for several days to express discontent with the budget agreement and a desire for a more conservative approach to federal spending. The House deadlock ended after meetings with Speaker McCarthy that redefined fiscal RFA funding levels as ceilings, not floors.
- House Appropriations Chair Kay Granger (R-TX) stated that the House will write their pending bills totaling $119 billion less than the FRA level (protecting defense and veterans). The Senate will write their bills in line with funding totals set by the FRA (FY 2023 levels). The House and Senate proposals will be very different, which will likely result in a challenging September-December period.
- The House plans to claw back $115 billion from unspent funds, which makes it difficult to predict final House allocations—the totals may be closer to Senate levels.
- Ms. Gibbons outlined the FY 2023 enacted funding and FY 2024 President's budget request. The funding proposals from the House and Senate will likely be very different. The President's budget request for FY 2024 would provide $716 million for the Cancer Moonshot and $2.5 billion for the Advanced Research Projects Agency for Health.
- The Senate Labor-Department of Health and Human Services (LHHS) NIH budget hearing, which was held on May 4, 2023, was bipartisan and emphasized the importance of investments in biomedical research across NIH. The House did not have a standalone NIH budget hearing—Dr. Tabak joined CDC leadership and HHS administration for preparedness and response leadership to testify at a House Labor-HHS subcommittee hearing focused on management of the COVID public health emergency.
- Ms. Gibbons shared updates from recent congressional briefings that NCI colleagues participated in including Drs. Amy LeBlanc and Stan Lipkowitz.
- Must-pass legislation with deadlines in September include the appropriations bills, FDA User Fee provisions for animal drugs, the Pandemic and All-Hazards Preparedness Act, and the Annual Defense Authorization Act.
- Potential competing priorities include oversight activity and drug pricing legislation.
- Ms. Gibbons ended by providing an overview of the 2023 Congressional calendar.

Discussion

- Ms. Ellis thanked Ms. Gibbons for the update and asked about the possibility of a continuing resolution (CR) in the future. Ms. Gibbons responded that the House and Senate will be working on the individual bills until the end of September, but it is not clear whether the deadline will be met. A CR is very likely. Government shutdowns are difficult to predict and the House turning back to FY 2022 levels may hinder progress.

- Ms. Ellis commented on recent Dear Colleague Letters on the cancer drug shortage and asked about any potential activity. Ms. Gibbons noted that there is a lot of interest in this issue and that a few hearings have been held. Different proposals have been presented that are focused on specific parts of the issue and solutions, but none have proposed a comprehensive solution. The competing priorities are a challenge. This is a system issue that cannot be entirely solved by the legislature.

Closing Remarks and Board Administration

Ms. Amy Williams and Ms. Annie Ellis

Dr. Willmarth made a motion to approve the minutes of the 88th NCRA meeting. Ms. Delgado Harris seconded the motion. The motion passed unanimously.

Ms. Ellis and Ms. Williams thanked Council members for their time and the work of OAR staff.

The next NCRA meeting is scheduled for October 4, 2023. The meeting was adjourned at 3:06 p.m. EST.

Certification

I hereby certify that foregoing minutes are accurate and complete.

October 12, 2023
Date

\s\
Annie Ellis
Chair
NCI Council of Research Advocates

October 12, 2023
Date

\s\
Amy Williams
Executive Secretary
NCI Council of Research Advocates