NCI Principal Deputy Director's Report

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Principal Deputy Director, National Cancer Institute

June 21, 2023

89th Meeting of the NCI Council of Research Advocates

@NCIDirector
@TheNCI

NIH NATIONAL CANCER INSTITUTE

Today's Talk

- Debt ceiling agreement & NCI budget
- Cancer Drug Shortages
- Research initiatives
- Research Advances
- Other topics

U.S. Debt Ceiling Agreement

- The debt limit deal signed into law at the beginning of the month would raise the debt limit until 2025.
- It would also impose caps on government spending for the next two fiscal years.
- Some areas would not face funding cuts (e.g., defense and veteran health care), but the overall non-defense discretionary funding level will be held at FY23 levels for the next fiscal year, and limited to a 1% increase in FY25.
- This will likely affect funding for many government agencies, including the NIH.

One Hundred Eighteenth Congress
of the
United States of America

AT THE FIRST SESSION

Begun and held at the City of Washington on Tuesday, the third day of January, two thousand and twenty-three

An Act

To provide for a responsible increase to the debt ceiling.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

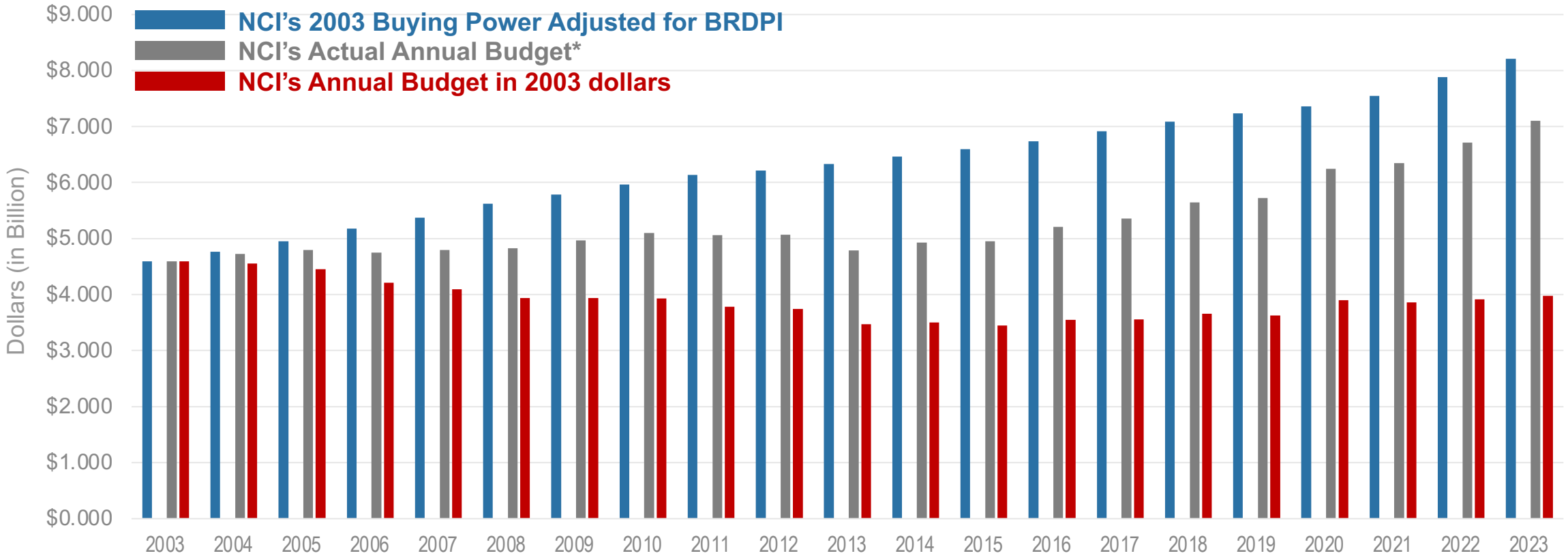
SECTION 1. SHORT TITLE.

This Act may be cited as the "Fiscal Responsibility Act of 2023".

Photo: President Biden signed the "Fiscal Responsibility Act of 2023" into law on June 3, 2023.
Content courtesy of MK Holohan, JD, Director, Office of Government and Congressional Relations, NCI

NCI's Budget Over Time

How does the 2023 NCI budget compare to 2003?



Content courtesy of Weston Ricks, Office of Budget and Finance, NCI
**Post transfers, excludes ARRA-H, 21st Century Cures Act funding, etc.*

President's NCI Budget for Fiscal Year 2024

$7.8B

Total President's budget proposal for NCI for FY 2024

+$502.9M

Total NCI budget increase for FY 2024

$716M

For Cancer Moonshot as no-year funds

$216M

Included for "Year 8" of 21st Century Cures Act Cancer Moonshot

$500M

Cancer Moonshot increase (relative to FY 2023 enacted level of $216M)

The Biden Administration is proposing a further increase of $1.45 billion in mandatory budget authority for FY25 and FY26.

CANCER MOONSHOT

PRESIDENT JOE BIDEN

Goals

- Reduce the cancer death rate by 50% in the next 25 years (in the U.S.)
- Overcome cancer disparities
- End cancer as we know it

Learn more: whitehouse.gov/moonshot
cancer.gov/moonshot

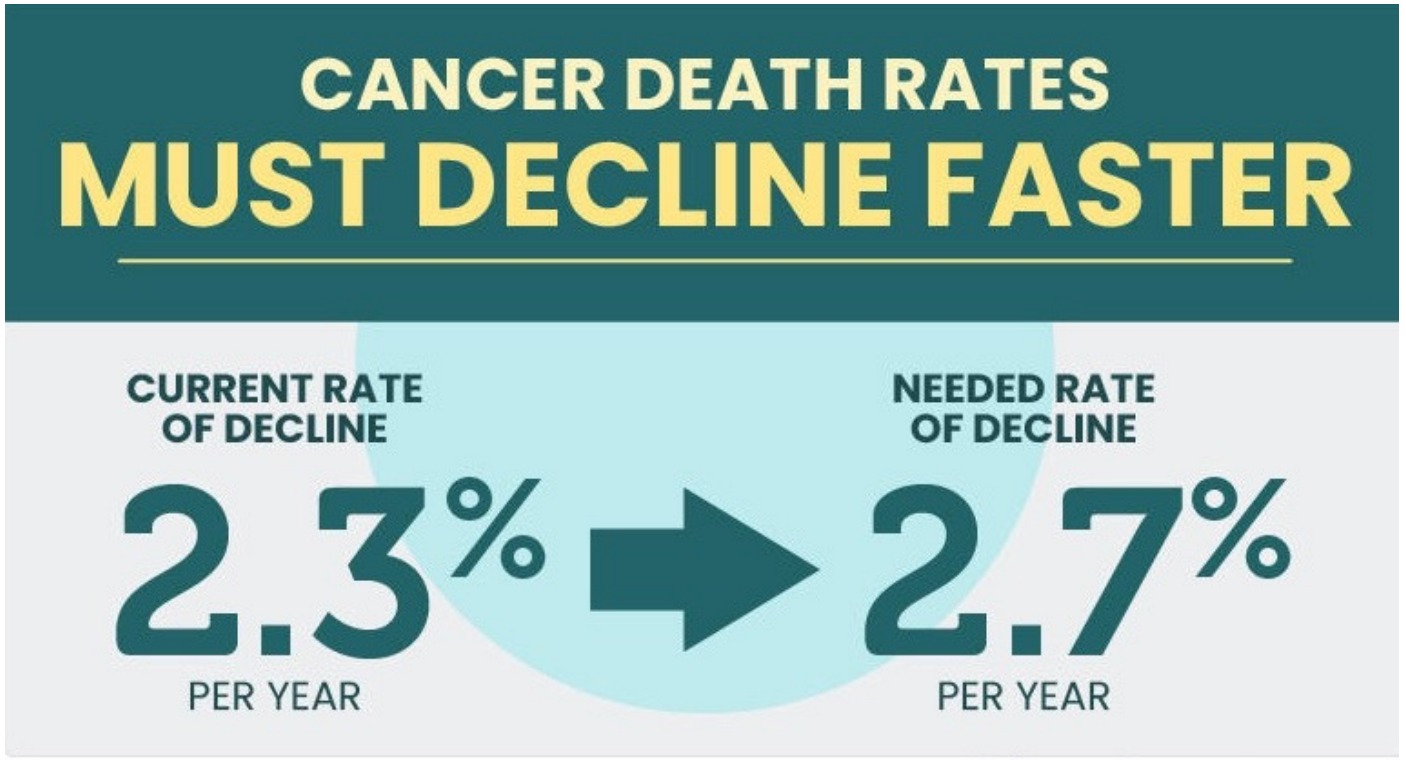
Achieving the Cancer Moonshot Goals

REDUCE CANCER MORTALITY BY AT LEAST

50%

over the next 25 years

and improve the experience of people and their families living with and surviving cancer.



SOURCE: Shiels M, et al. *Cancer Discovery*. 2023

TUESDAY, JUNE 20, 2023 · THE WASHINGTON POST E5

LIFE WITH CANCER

Cancer patients confront shortages of chemotherapy drugs

BY RENE EBERSOLE

Oncology agents currently listed in FDA's Drug Shortages Database:

- **Azacytidine** for Injection
- **Capecitabine** Tablets
- **Carboplatin** Injection
- **Cisplatin** Injection
- **Cytarabine** Injection
- **Dacarbazine** Injection
- **Fludarabine Phosphate** Injection
- **Leucovorin Calcium** Lyophilized Powder for Injection
- **Methotrexate** Injection

Data updated as of May 22, 2023

Data courtesy of James H. Doroshow, MD (NCI Deputy Director for Clinical and Translational Research)

Estimated number of trials* with oncology agents currently in short supply

Current Trial Status	ETCTN	NCTN	Consortia (AMC, PBTC, CITN, PEP-CTN)	CCR	Formulary	Old N01 ETCTN	NHLBI	Grand Total
Active	12	69	2	1	0	0	1	85
Temporarily Closed to Accrual	2	11	3	0	0	0	0	16
Closed to Accrual	2	38	0	0	0	3	0	4
Approved	0	4	0	0	0	0	0	4
Approval on Hold	2	9	0	0	1	0	0	12
In Review	1	9	0	0	0	0	0	10
Grand Total	**19**	**140**	**5**	**1**	**1**	**3**	**1**	**170**

**Trials supported/sponsored by NCI's Cancer Therapy Evaluation Program (CTEP)*
Data updated as of May 22, 2023
Data courtesy of James H. Doroshow, MD (NCI Deputy Director for Clinical and Translational Research)

Estimated number of studies with shortage list oncology agents on protocol

No. of shortage list agents on protocol	No. of Studies
One (1) shortage agent on protocol	104
Two (2) shortage agents on protocol	47
Three (3) shortage agents on protocol	16
Four (4) shortage agents on protocol	3
Grand Total	**170**

**Trials supported/sponsored by NCI's Cancer Therapy Evaluation Program*
Data updated as of May 22, 2023
Data courtesy of James H. Doroshow, MD, NCI Deputy Director for Clinical and Translational Research

Clinical Trials Innovation Unit (CTIU):
Better, faster, more accessible cancer clinical trials

The CTIU will:

- **Select a few high-priority studies** for new study designs and operational procedures
- **Help speed clinical testing to deliver new approaches** for diagnosis, treatment, and prevention of cancer
- **Accept inputs** from the extramural research community
  - ✓ First proposal submission deadline: June 12

A collaboration between NCI, the FDA Oncology Center of Excellence, and the NCTN Group Chairs

ComboMATCH: Combination Therapy Platform Trial with Molecular Analysis for Therapy Choice

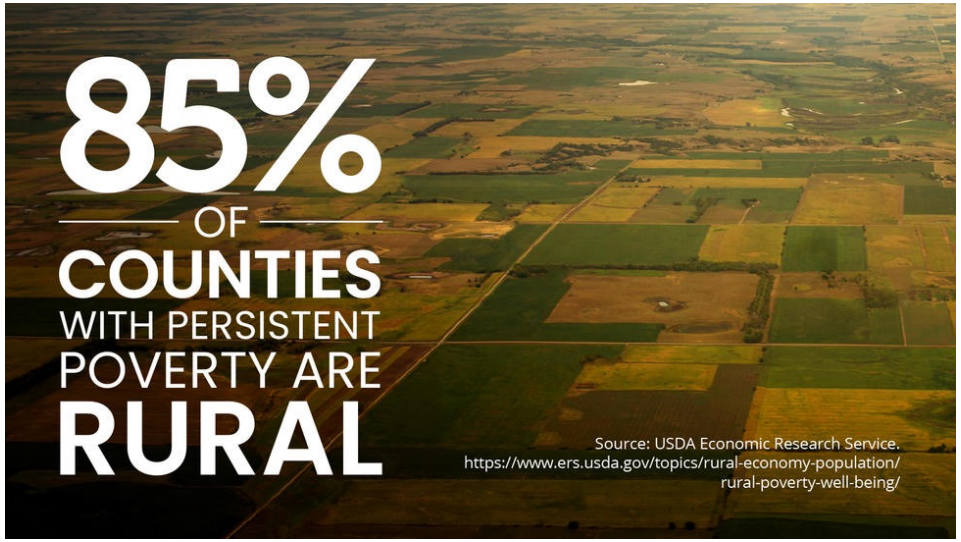
Trials open for enrollment	
Combination therapy trial	***Patients matched to trial***
Fulvestrant (Faslodex) and binimetinib (Mektovi)	Patients with an NF1 mutation in hormone receptor-positive breast cancer that has spread
Selumetinib (Koselugo) and olaparib (Lynparza) or selumetinib alone	Women with a RAS mutation who have endometrial or ovarian cancer that has come back or persists despite treatment
Chemotherapy plus ipatasertib	Patients with AKT mutations who have solid tumors that have spread

Plans:

- *6 trials to be available in coming months (more over time)*
- *Include ~2,000 patients*

Persistent Poverty Initiative

- $50 million to improve cancer outcomes in low-income areas by:
  - Building research capacity
  - Fostering cancer prevention research
  - Promoting the implementation of community-based programs
- Awards will fund **5 new Centers for Cancer Control Research in Persistent Poverty Areas** ($10 million over 5 years)
- First major program to address the structural and institutional factors of persistent poverty in the context of cancer



Funding Opportunity Announcement Number: ***RFA-CA-22-015***

Some highlights from National Clinical Trials Network (NCTN)

Content/data courtesy of:

Meg Mooney, MD, MS, Associate Director, Cancer Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute

Key Accomplishment:
Conduct of Collaborative Trials in Special Populations - AYA

S1826: Phase 3 Randomized Study of Nivolumab + AVD or Brentuximab Vedotin + AVD in Patients (Age >/= 12 Years) with Newly Diagnosed Advanced Stage Classical Hodgkin Lymphoma

Study Opened: July 2019
Study Closed: Dec 2022
994 Patients Enrolled (M/F: 45% vs 55%)

- **12 – 17 yrs: 24%**
- **18 – 60 yrs: 66%**
- **Over 60 yrs: 10%**

White 76%, Black, 12%, Asian 3%; Hispanic 13%

Results Presented 2023 ASCO Plenary Session

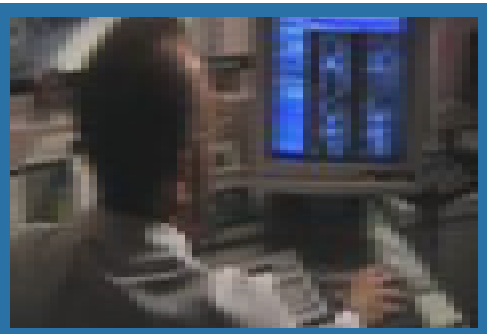
J Clin Oncol 41, 2023 (suppl 17; abstr LBA4)

- N-AVD improved progression-free survival (PFS) compared to Bv-AVD as initial treatment of advanced stage cHL
- N-AVD was well-tolerated
  - Few immune-related adverse events
  - < 1% of patients received radiation therapy (RT)
- Key step towards harmonizing pediatric and adult therapy of cHL
- **N-AVD is poised to be a new standard for treatment of advanced stage cHL**

Key Accomplishment:
Question Not Well-supported in a Commercial Environment

PROSPECT: Alliance N1048

PreOp Chemotx w/ Selective ChemoRT *versus* ChemoRT for Patients with Locally Adv Rectal Cancer



Study Activation: Jan 2012
Closed Accrual/Tx: Nov 2019
Total Enrollment: 1,194 patients

Non-inferiority Trial

Compare standard 5FUCMT to neoadjuvant FOLFOX followed by selective use of 5FUCMT with respect to the co-primary endpoints of Time to Local Recurrent & Disease-free Survival

Most Intermediate rectal cancer patients can receive curative-intent treatment without pelvic chemoradiation

- **Clinical Correlatives:** Quality of Life (QOL) & Patient Report Outcomes (PROs)
- **Immunologic Studies:** Indicators of Immunologic Activation
- **Pharmacogenomics:** Germline Variation as a Predictor of Response & Toxicity to Platinum-based Chemotx & RT

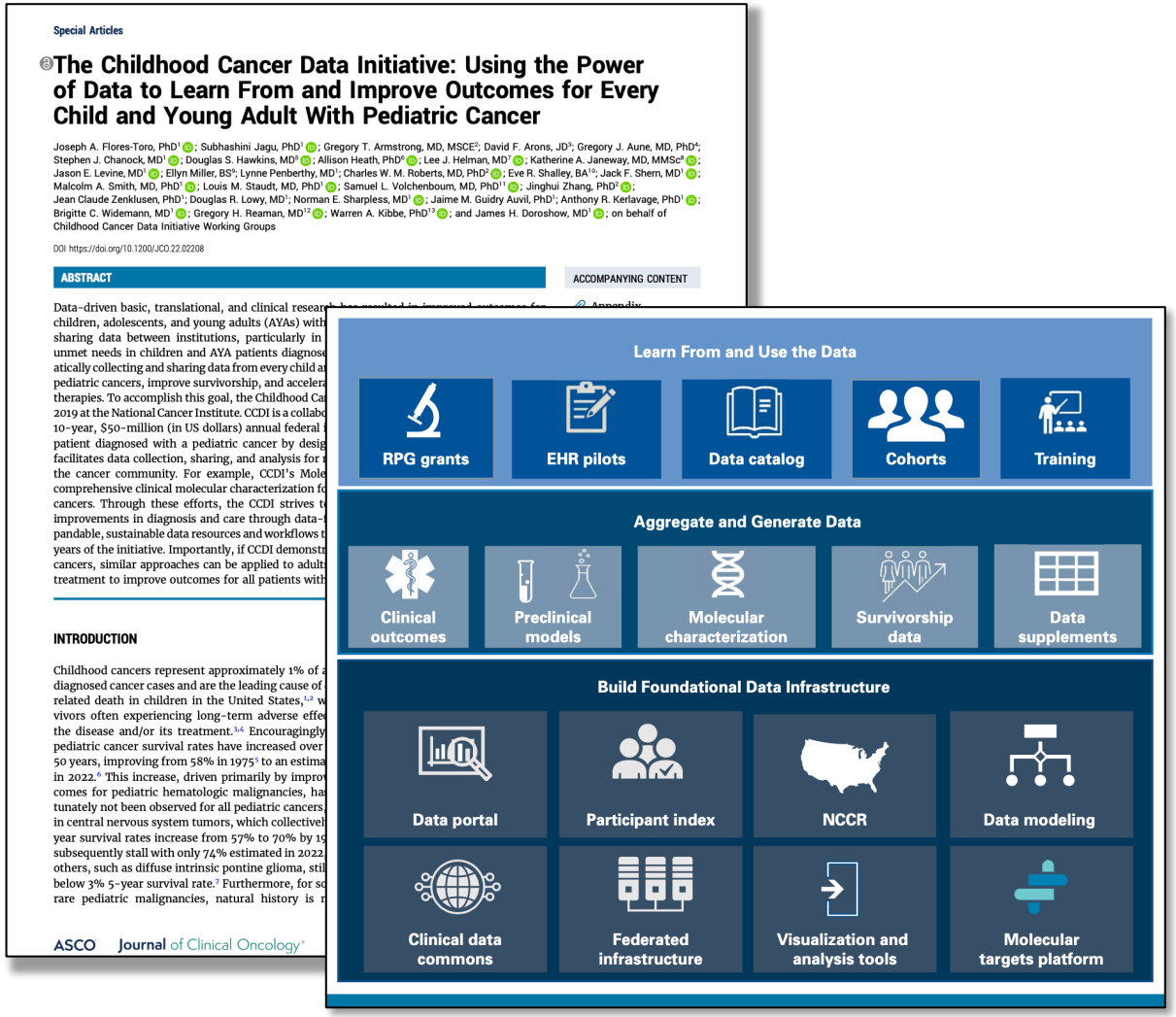
Results Presented 2023 ASCO Plenary Session & Simultaneous NEJM Publication

J Clin Oncol 41, 2023 (suppl 17; abstr LBA2)

Other Selected Recent Key Accomplishments - Results

Trial	Impact / Accomplishment
AHOD1331: Randomized Phase 3 Study of Brentuximab Vedotin for Newly Dx'ed **High-Risk Classical Hodgkin Lymphoma in Children & Young Adults**	Patients receiving brentuximab vedotin with chemotherapy had a **Superior 3-year Event-Free Survival** (92.1%) compared to those who did not receive the agent (82.5%) with no increase in toxicity. **NEJM Publication & FDA Approval of Indication Nov 3, 2022.**
E1910: Phase 3 Randomized Trial of Blinatumomab for Newly Diagnosed BCR-ABL-Negative B Lineage **Acute Lymphoblastic Leukemia in Adults**	Blinatumomab added to consolidation chemotherapy led to significantly **Better Overall Survival** in pts with newly dx'ed B-cell ALL who were MRD negative after intensification chemotx (median OS: not reached vs 71.4 months, HR 0.42, 95% CI: 0.24 - 0.75; two-sided p=0.003). Median F/U of 43 months. Represents new standard for BCR::ABL1 negative ALL adult patients 30-70 yrs. **Late Breaking Abstract Session ASH Annual Mtg Dec 6, 2022. Designed as a Registration Intent Study for FDA Approval in Indication.**
NRG-GY018: Randomized, Placebo-Controlled Study of Pembrolizumab in Addition to Paclitaxel & Carboplatin for Measurable Stage III or IVA, Stage IVB or **Recurrent Endometrial Cancer**	Pembrolizumab in combination with chemotherapy resulted in a significantly **improved Progression-free Survival (PFS)** in dMMR cohort of 74% compared to 38% in placebo group (HR, 0.30; 95% CI 0.19 to 0.48; P<0.001). In pMMR cohort, median PFS was 13.1 months *vs* 8.7 months (HR, 0.54; 95% CI, 0.41 to 0.71; P<0.001). **Presented Annual SGO Mtg with NEJM publication on Mar 27, 2023. Designed as Registration Intent Study for FDA Approval in Indication.**

The Childhood Cancer Data Initiative (CCDI): Using the Power of Data to Learn From and Improve Outcomes for Every Child and Young Adult With Pediatric Cancer



- The paper explains CCDI's **accomplishments** to date and discusses **priorities** for the future of the initiative.
- Its publication is an important milestone for raising awareness among clinicians, academic researchers, and others about CCDI data sharing efforts.

Flores-Toro JA, et al. Journal of Clinical Oncology. June 2, 2023.

RNA-based Cancer Vaccines

Request for Information

Responses will be used to inform future resource allocation and acquisition strategies that can accelerate the development, availability, and evaluation of such agents.

Send responses and questions to Dr. Andrew Kurtz at **nciRNAvaccines**@mail.nih.gov

NOTICE NUMBER:
NOT-CA-23-063

Needs and Challenges in Obtaining and Testing Clinical-Grade RNA-based Cancer Vaccine Formulations to Support Translational and Clinical Research

Responses due by June 30, 2023

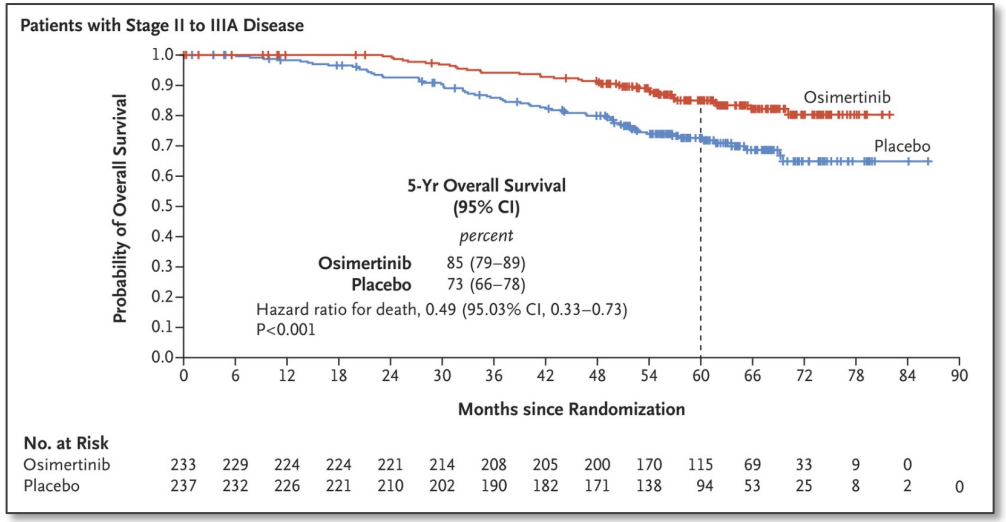
Phase 3 trial shows survival benefit of targeted treatment for patients with resected EGFR-mutated NSCLC

Results:

- Adjuvant osimertinib provided a **significant overall survival benefit** among patients with completely resected, EGFR-mutated, stage IB to IIIA non-small cell lung cancer.

About the trial:

- Phase III double-blind trial
- Primary endpoint: Disease-free survival
- Participants:
  - Randomized (stage II to IIIA)
  - Overall population (stage IB to IIIA)
- Funded by AstraZeneca
  - ADAURA ClinicalTrials.gov number: NCT02511106



5-year overall survival		
Stage	**Osimertinib**	**Placebo**
II to IIIA	**85%**	73%
IB to IIIA	**88%**	78%

Tsuboi M, et al. *New England Journal of Medicine*. June 4, 2023.

Increasing access to cancer care & control
Some parting ideas…

- NCI does ***not*** set health care delivery policy
- But…**NCI can work with other groups** to help achieve wider and more equitable dissemination/access to health care delivery, an important goal of the Cancer Moonshot
- A possible example: Access to and uptake of tumor DNA sequencing, where recommended by guidelines

Thank you!

www.cancer.gov

www.cancer.gov/espanol

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