

MESSAGE FROM DCTD'S DIRECTOR AND DEPUTY DIRECTOR



Jim Doroshow, MD
 Director, DCTD
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Each quarter, DCTD's newsletter highlights the scientific interests and research efforts of one of our many talented staff members. We would like to dedicate this edition to the individuals who continue to have a positive impact on cancer research during the challenges presented by the COVID-19 pandemic. Thank you to NCI staff who are supporting our mission during this unprecedented and difficult time. We appreciate all NCI-supported basic and clinical researchers who are dedicated to improving the lives of people with cancer. And, to the individuals living with cancer, including those enrolled on NCI-supported clinical trials, we want to emphasize that your health remains NCI's priority. We are working with NCI investigators across the U.S. during this continuously evolving situation to maintain patient access to critical treatments and care.



Toby Hecht, PhD
 Associate Director,
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 Deputy Director, DCTD

As we move forward through spring, we, as cancer researchers, are learning that a key response to COVID-19 is to adapt. A [series of memoranda](#) were developed

in mid-March, led by Drs. Wortá McCaskill-Stevens in NCI's Division of Cancer Prevention (DCP) and Meg Mooney in DCTD's Cancer Therapy Evaluation Program (CTEP), that address how individual investigators at sites in NCI's National Clinical Trials Network (NCTN) and NCI's Community Oncology Research Program (NCORP) can help patients adjust to this new environment. A broader range of clinical trial activities— physical exams, performance assessments, research blood collection, and some imaging modalities—can now be performed by the patients' local physician so that patients do not need to travel to a clinical center. The U.S. Food and Drug Administration and the NCI CTEP Pharmaceutical Management Branch have made it easier to have a site's dispensing pharmacy ship appropriate oral investigational agents used in CTEP IND studies directly to the patients. We are also working to ensure that the effects of the pandemic do not compromise data evaluation in ongoing trials, recognizing that it may be extremely

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challenging to collect research samples. This is a remarkable time, and the NCI will be flexible.

NCI has also moved swiftly to develop a national, longitudinal, natural history study of COVID-19 in people with cancer: [the NCI COVID-19 in Cancer Patients Study \(NCCAPS\)](#) was launched in May. This study, which was collaboratively developed by staff in NCI's DCP and in CTEP by Dr. Larissa Korde and Andrea Denicoff with extramural investigators from Vanderbilt University Medical Center, is open to adults who have tested positive for COVID-19 and are undergoing cancer treatment that requires them to go to a healthcare facility to receive their cancer treatment. NCCAPS will be open to children who also have tested positive for COVID-19 and have cancer as well. We hope to enroll patients at more than 1,000 sites across the U.S. through the NCTN, NCORP, and NCI Experimental Therapeutics Clinical Trials Network (ETCTN). The goals of the study are to:

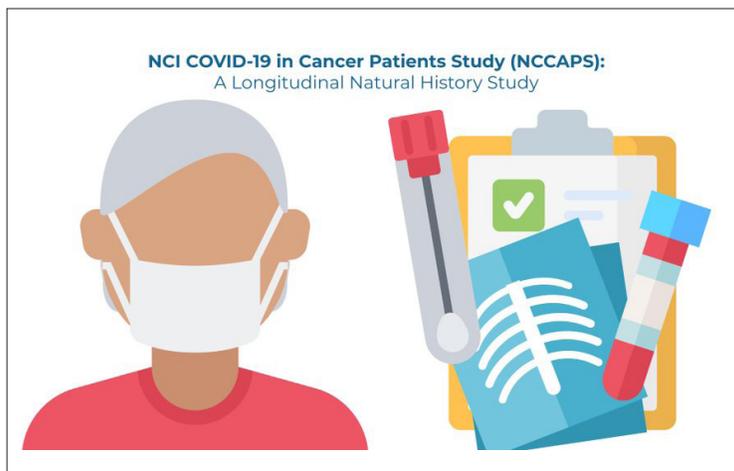
- Help scientists better understand the natural history of COVID-19 in people with cancer
- Collect comprehensive longitudinal data, imaging scans, and serial blood specimens, and build a clinical database and repository of these data
- Investigate how COVID-19 affects cancer treatment and cancer outcomes
- Identify clinical and molecular factors associated with severe COVID-19 and mortality
- Assess long-term effects of COVID-19 on cancer outcomes and quality of life

NCI is also launching an expanded access protocol for tocilizumab, an interleukin-6 (IL-6) receptor antagonist, to treat up to 200 cancer patients who have been diagnosed with COVID-19 and are experiencing severe respiratory symptoms. This drug may help

treat a hyperactive immune response that has been documented in patients with COVID-19. Led by CTEP's Drs. Richard Little and Nirali Shah in NCI's Center for Cancer Research, the protocol was drafted by NCI investigators in less than one week. We are working with Genentech, the

drug's manufacturer, and launched the study in May. One objective of this trial is to find out whether this therapy decreases the time cancer patients with severe COVID-19 spend in the intensive care unit.

Although the pace of cancer research may be altered during this time, many of NCI/DCTD's research efforts continue. For example, with support from DCTD, the NCI Biopharmaceutical Development Program at Frederick National Laboratory for Cancer Research (FNLCR) is facilitating the [manufacture of CD33 CAR-T cells](#) for a multicenter clinical trial in pediatric patients with acute myeloid leukemia. A milestone was reached in late March when the first patient was treated with CAR-T cells manufactured at FNLCR. In addition, NCI recently began requesting letters of intent for laboratories to participate in the [NCI-ComboMATCH](#) clinical trial, the first successor trial of NCI-MATCH. Approved designated labs will test tumor specimens to identify patients for specific gene abnormalities needed for trial eligibility. NCI-ComboMATCH will evaluate targeted drug combinations in part based on preclinical *in vivo* evidence of activity.



MESSAGE FROM ... continued

While NCI adapts to the evolving public health challenges of COVID-19, we extend our gratitude to everyone making this possible.

Patients and researchers can access the latest information and guidance from NCI on COVID-19 using the links at the top of [NCI's website](#).

SPOTLIGHT – The NCI Formulary Expands to Offer 31 Agents from 10 Companies



- Following company approval, investigators can obtain NCI Formulary agents and test them in new preclinical or clinical studies, including combination studies of Formulary agents from different companies.
- The NCI Formulary was launched on January 11, 2017 ([NCI press release](#)) with six participating companies and has expanded to include the following 10 companies offering 31 targeted agents:

The [NCI Formulary](#) is a public-private partnership between NCI and pharmaceutical and biotechnology companies that offers investigators at NCI-audited clinical research centers in the U.S. who are main member sites of the NCI National Clinical Trials Network and the Experimental Therapeutics Clinical Trials Network rapid access to agents or combinations of agents for clinical research or to any U.S. investigators for preclinical research.

- Amgen
- AstraZeneca
- Bayer
- Bristol-Myers Squibb
- Eli Lilly and Company
- EMD Serono
- Genentech
- Kyowa Hakko Kirin Co, Ltd.
- Syntrix Biosystems, Inc.
- Xcovery Holding Company LLC

NCI Formulary Facts

- The availability of agents through the NCI Formulary expedites the start of clinical trials by alleviating the lengthy agreement negotiation process—sometimes up to 18 months—that has been required for investigators to access such agents on their own.

SPOTLIGHT – NCI Requests Letters of Intent for Laboratories to Participate in the NCI-ComboMATCH Clinical Trial

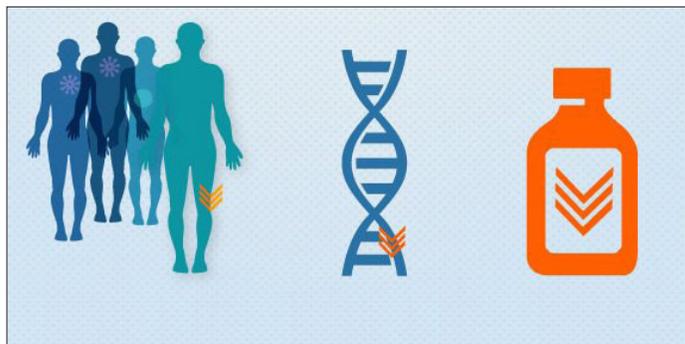
NCI and the ECOG-ACRIN Cancer Research Group (ECOG-ACRIN) are developing **NCI-ComboMATCH**, a successor precision medicine trial to **NCI-MATCH**. ComboMATCH will concentrate on targeted drug combination signal-seeking studies supported by preclinical *in vivo* evidence.

NCI-ComboMATCH trial leadership invites applications for Clinical Laboratory Improvements Program (CLIA) certified/ accredited laboratories that test tumor specimens from patients utilizing Next-Generation Sequencing (NGS) assays to participate in the NCI-ComboMATCH trial.

NCI has published two solicitations for the recruitment of CLIA accredited laboratories to support NCI-ComboMATCH:

1. **Laboratory sites identifying cases from the general population**
2. **Laboratory sites identifying exclusively pediatric cases**

These laboratories will join a **network of 30 designated laboratories** already put in place last year to identify cases for NCI-MATCH.



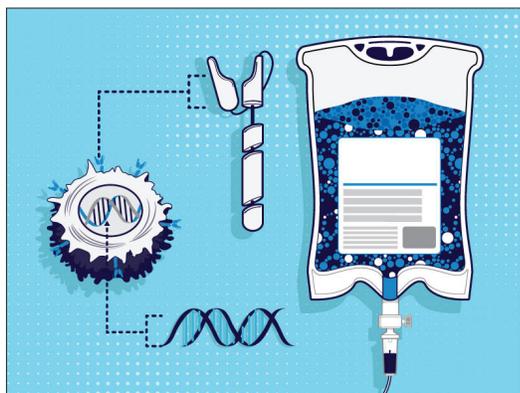
To support ComboMATCH, the designated laboratories will identify patients for the specific gene abnormalities needed for trial eligibility using assays performed as standard-of-care. Laboratories will be required to contact any of the National Clinical Trial Network sites that have activated NCI-ComboMATCH if a specimen sent from one of these sites has a gene abnormality that would potentially make the patient eligible for one of the treatment arms.

Applicants have until 5:00 PM on June 30, 2020 to submit their letters of intent.

NEWS ABOUT DCTD PROGRAMS AND ACTIVITIES

Program Updates

First Patients Treated with Cell-based Immunotherapy Manufactured at FNLCR



DCTD is supporting the production of cell-based immunotherapies at NCI, allowing NCI to make cell therapy products available to intramural and extramural clinical trial investigators. NCI is supporting a multicenter clinical trial ([NCT03971799](#)) of CD33 CAR-T cells in pediatric acute myeloid leukemia. The first two patients enrolled on this trial received treatment this spring.

The NCI Biopharmaceutical Development Program at Frederick National Laboratory for Cancer Research (FNLCR) is currently positioning itself to facilitate multicenter phase 1/2 cell-based immunotherapy clinical trials by:

- Providing centralized manufacturing of cell-based products in a current GMP (cGMP) facility
- Ensuring consistent and standardized manufacturing processes, increasing reproducibility

Updates on NCI-COG Pediatric MATCH

NCI-COG Pediatric MATCH is a nationwide cancer treatment clinical trial for children and adolescents, from 1 to 21 years of age, which is testing the use of precision medicine for pediatric cancers. The trial seeks to find out whether it is effective to treat cancer in children and adolescents by targeting certain genetic changes in their tumors with specific targeted drugs, no matter the type of cancer or cancer site. Tumors will be tested for changes in more than 160 genes related to cancer.

Launched in July 2017, the trial planned to screen 200-300 patients per year for a total of 1,000 patients. This spring, the trial expanded its screening goal to 1,500 patients. The trial will

- Addressing product chain logistical issues

Facility renovations that are underway will allow for vector production (lentivirus and retrovirus) to begin in 2020 and for new cell therapy suites to come online in late 2021 that will triple the capacity for production of cell therapy and vector products.

Read more about [DCTD's](#) and [NCI's](#) support of cell therapy production.



also add three new arms this year for a total of 13, after launching with seven arms at the time the study began.

Radiopharmaceutical Development Initiative (RDI)



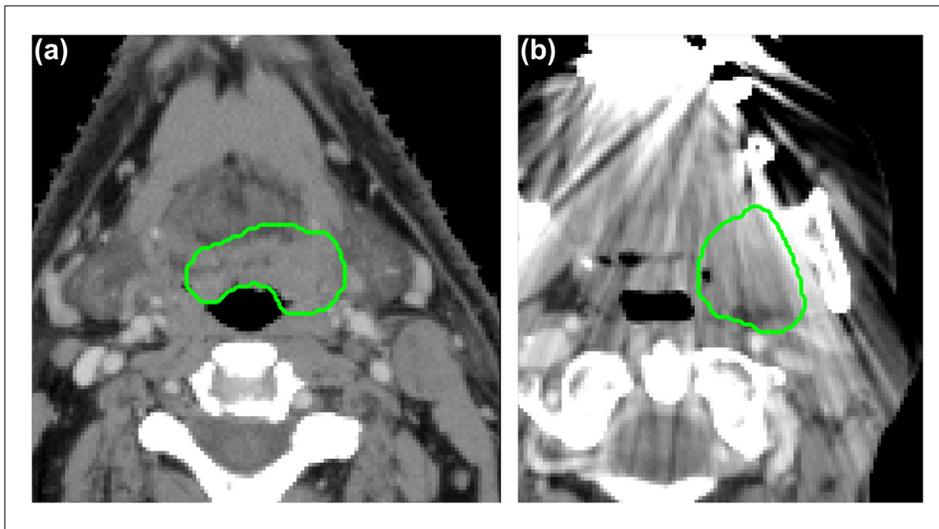
As part of NCI's overall drug development efforts in collaboration with the pharmaceutical industry and academic investigators, NCI has developed a specialized infrastructure, the Radiopharmaceutical Development Initiative (RDI), for the clinical evaluation of novel theranostic radiopharmaceutical cancer therapies. The focus of NCI's efforts is to complement industry development of these agents with early phase combination studies to test tolerability and early signs of efficacy of

radiopharmaceutical agents in combination with other novel agents that may add to their clinical benefit. RDI radiopharmaceutical-based trials involve both early phase and late phase

clinical studies of cancer treatments in high priority areas of unmet medical needs. [Read more about the RDI.](#)

Highlights from the Cancer Imaging Archive (TCIA)

- The TCIA collections are enriched by its user community of researchers who are encouraged to contribute back their [analysis of existing collections](#). A new interface that makes it easy to find almost 30 sets of user-contributed segmentations, quantitative features, and analysis results was released this month.
- The recently published [OPC-Radiomics collection](#) contains radiotherapy planning CTs, RTSTRUCT gross tumor volume contours, and clinical outcomes from 606 patients with oropharynx cancer.
- On March 18, the [TCIA image hosting and research activities](#) related to the Clinical Proteomic Tumor Analysis Consortium were presented as part of an Office of Cancer Clinical Proteomics Research Webinar series.
- [Data from the ACRIN-HNSCC-FDG-PET/CT \(ACRIN 6685\) clinical trial](#) are now available for access by NCI's Quantitative Imaging Network investigators.



Representative images demonstrating gross tumor volume (shown in green) without (a) and with (b) visible CT artifacts.

Publications and Outreach

Publications

Levy EB, Fiel MI, Hamilton SR, et al. [State of the Art: Toward Improving Outcomes of Lung and Liver Tumor Biopsies in Clinical Trials- A Multidisciplinary Approach](#). *J Clin Oncol*. 2020 May 10;38(14):1633-1640.

O'Sullivan Coyne G, Wang L, Zlott, et al. [Intravenous 5-fluoro-2'deoxyctidine Administered with Increases the Proportion of p16-expressing Circulating Tumor Cells in Patients with Advanced Solid Tumors](#). *Cancer Chemother Pharmacol*. 2020 May;85(5):979-993.

Conley BA, Staudt L, Takebe N, et al. [The Exceptional Responders Initiative: Feasibility of A National Cancer Institute Pilot Study](#). *J Natl Cancer Inst*. 2020 Apr 27. Epub ahead of print.

Kurmasheva RT, Bandyopadhyay A, Favours E, et al. [Evaluation of VTP-50469, a menin-MLL1 Inhibitor, against Ewing Sarcoma Xenograft Models by the Pediatric Preclinical Testing Consortium](#). *Pediatr Blood Cancer*. 2020 Apr 25. Epub ahead of print.

Chauhan A, Kabir T, Wu J, et al. [Prognostic and Predictive Factors Associated with Ipilimumab-related Adverse Events: A Retrospective Analysis of 11 NCI-sponsored Phase I Clinical Trials](#). *Oncotarget*. 2020 Apr 21;11(16):1427-1434.

Rozenblatt-Rosen O, Regev A, Oberdoerffer P, et al. [The Human Tumor Atlas Network: Charting Tumor Transitions across Space and Time at Single-Cell Resolution](#). *Cell*. 2020 Apr 16;181(2):236-249.

Johnson DB, Zhao F, Noel M, et al. [Trametinib Activity in Patients with Solid Tumors and Lymphomas Harboring BRAF Non-V600 Mutations or Fusions: Results from NCI-MATCH \(EAY131\)](#). *Clin Cancer Res*. 2020 Apr 15;26(8):1812-1819.

Gross AM, Wolters PL, Dombi E, et al. [Selumetinib in Children with Inoperable Plexiform Neurofibromas](#). *N Engl J Med*. 2020 Apr 9;382(15):1430-1442.

Zakeri K, Narayanan D, Prasanna P, et al. [Development of Novel Radiosensitizers through the National Cancer Institute's Small Business Innovation Research Program](#). *Radiat Res*. 2020 Mar 27. Epub ahead of print.

Evrard YA, Srivastava A, Randjelovic J, et al. [Systematic Establishment of Robustness and Standards in Patient-Derived Xenograft Experiments and Analysis](#). *Cancer Res*. 2020 Mar 9. Epub ahead of print.

Merino DM, McShane LM, Fabrizio D, et al. [Establishing Guidelines to Harmonize Tumor Mutational Burden \(TMB\): In Silico Assessment of Variation in TMB Quantification across Diagnostic Platforms: Phase I of the Friends of Cancer Research TMB Harmonization Project](#). *J Immunother Cancer*. 2020 Mar;8(1).

NCI Cancer Currents Blog Posts



[How Does COVID-19 Affect People with Cancer? NCI Plans to Find Out](#); James Doroshov, MD; May 21, 2020.

[PSMA PET-CT Accurately Detects Prostate Cancer Spread, Trial Shows](#); Lalitha Shankar, MD, PhD, Cancer Imaging Program; May 11, 2020.

[Encorafenib, Cetuximab Combination Approved for Metastatic Colorectal Cancer](#); Carmen Allegra, MD, Cancer Therapy Evaluation Program; May 8, 2020.

[NCI Initiative Aims to Boost CAR T-cell Therapy Clinical Trials](#); Anthony Welch, PhD, Developmental Therapeutics Program; April 23, 2020.

Interviews and Press

[Tumor Molecular Profiling May Help Identify “Exceptional Responders”](#); Percy Ivy, MD, Cancer Therapy Evaluation Program; Medscape; May 20, 2020.

[Covid-19 Stalls Clinical Trials for Everything but Covid-19](#); Lyndsay Harris, MD, Cancer Diagnosis Program; Wired; April 17, 2020.

[IGF-1R Drugs Travel from Cancer Cradle to Graves'](#); Helen Chen, MD, Cancer Therapy Evaluation Program; Nature Biotechnology; April 7, 2020.

[NCI Statement on Clinical Trials during COVID-19 Pandemic](#); NCI Press Release; March 19, 2020

[In NIH Trial, Selumetinib Shrinks Tumors, Provides Clinical Benefit for Children with NF1](#); NCI Press Release; March 18, 2020.