

Developmental Therapeutics Clinic

Early Phase Clinical Trials Program

Division of Cancer Treatment and Diagnosis (DCTD)

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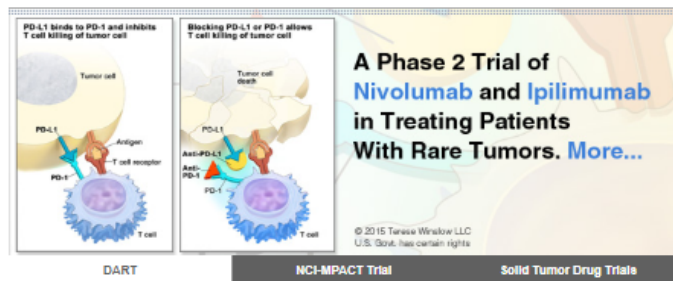
July 12th, 2019

Developmental Therapeutics Clinic (DTC)

- DTC is part of the Division of Cancer Treatment and Diagnosis, tasked with early drug development of novel agents, particularly in the exploration and confirmation of mechanism of action.
- DTC conducts early-phase trials of novel agents with correlative pharmacokinetic and pharmacodynamic endpoints
- The DTC works in concert with NCI's Experimental Therapeutics Program (NExT)
 - Drug discovery and development initiative



DTC Developmental Therapeutics Clinic



Welcome to the Developmental Therapeutics Clinic

The goal of the National Cancer Institute (NCI) Developmental Therapeutics Clinic (DTC) is to develop new treatments for patients with advanced cancer through innovative early-phase clinical trials. This clinic focuses on rationally developing new drugs and drug combinations that target specific abnormalities in tumors, rather than on one cancer type or histology. DTC staff utilize the power of molecular, precision medicine to design clinical trials that can help evaluate the benefit of the proposed therapy. DTC is part of the NCI, which is one of 27 institutes and centers that comprise the National Institutes of Health (NIH). DTC participates in the [Experimental Therapeutics Clinical Trials Network \(ETCTN\)](#) and supports the work of the Division of Cancer Treatment and Diagnosis (DCTD).

Each year, patients from around the world with cancers that have relapsed after standard treatment visit DTC for consultation about participation in the innovative new treatment trials conducted at NIH. DTC treats patients in the [NIH Clinical Center](#), and DTC staff collaborate with the patient's current clinical provider to ensure outstanding clinical care. Our patients are referred by other patients, patient's physicians, families and friends, or personally may seek out these studies independently.

If you are a referring physician, patient, or family member, please [contact us by email or phone](#).

Clinical Trials Questions?

Speak with a DTC Patient Coordinator

General Cancer Questions?

Speak with NCI's Cancer Information Service

Tweets by @NCITreatment



News

DTC Offers Fellowship Opportunities

Arjun Mitra, MD, DTC Advanced Fellow, Receives Conquer Cancer Foundation 2015 ASCO Annual Meeting Merit Award

Three DTC Staff Presentations at AACR 2015:

– Phase I Trial of Recombinant Human Interleukin 15 (rhIL-15) In Combination with Nivolumab and Ipilimumab in Refractory Cancers

– DNA Damage Response and Therapeutic Activity following Once-daily Administration of the Wee 1 Inhibitor AZD1775 (adavosertib)

– A Phase II Trial of TRC102 (methoxyamine HCl) In Combination with Temozolomide in Patients with Relapsed



PDMR

NCI Patient-Derived Models Repository
An NCI Precision Oncology Initiative™ Resource



CTEP Cancer Therapy Evaluation Program





DTC Developmental Therapeutics Clinic

[Clinical Trials List](#)
[Clinical Trials Q&A](#)
[Clinical Trials Contacts](#)

Clinical Trials

Last Updated: 05/09/19

Clinical Trials List

These are the trials that are currently offered at our clinic.

Tumor Type

- ▶ All Cancer Types
- ▶ Sarcoma
- ▶ Lymphoma
- ▶ MDS
- ▶ Rare Tumors

[^ Back to Top](#)

Trial Type

- ▶ Immunotherapy
- ▶ Precision Medicine

[^ Back to Top](#)

Trial Phase

- ▶ Phase 1
- ▶ Phase 2

Clinical Trials Questions?

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▼ MDS

- **Phase I Trial of the Combination of Bortezomib and Clofarabine in Adults with Refractory Solid Tumors**

DTC Trials: Planned MDS cohort inclusion for Aza-TdC

- Nucleoside analog 5-aza-4'-thio-2'-deoxycytidine
- DNA methyltransferase 1 (DNMT1) inhibitor

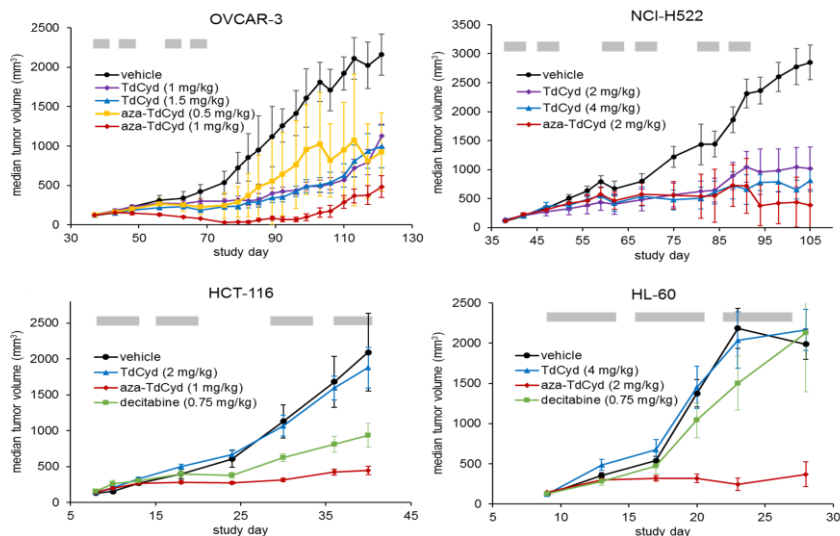
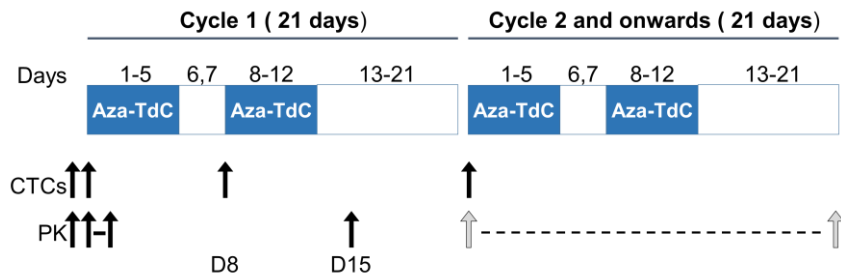


Figure 1. Efficacy of Aza-TdC (aza-TdCyd) and TdCyd in human tumor xenograft models.



Study Objectives:

- Safety, tolerability, and maximum tolerated dose (MTD) of oral Aza-TdC administered daily for 5 days a week for 2 weeks, with one week off, in 21-day cycles, to patients with refractory solid tumors
- Determine the pharmacokinetics, pharmacodynamics (gene re-expression) and preliminary activity of oral Aza-TdC

Dose Level	Aza-TdC, mg
-1	1
1	2
2	4
3	8
4	16
5	32
6	64
7	128

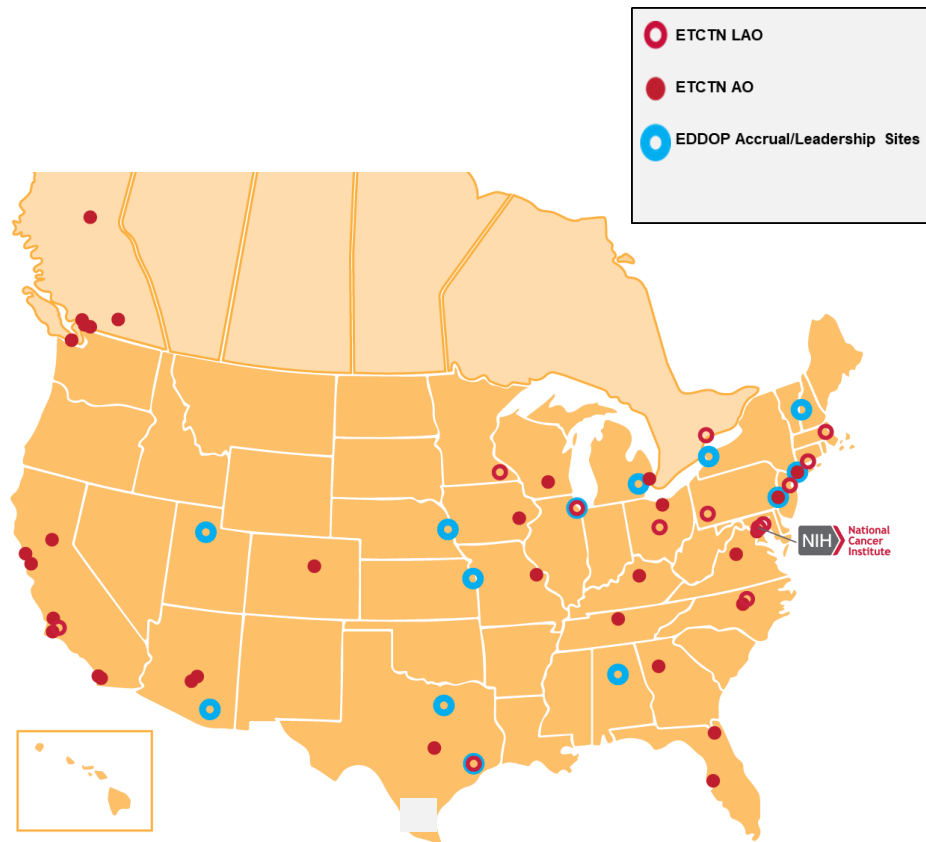
Experimental Therapeutics Clinical Trials Network

Experimental Therapeutics Clinical Trials Network (ETCTN)

- The National Cancer Institute (NCI) has formed partnerships in the pharmaceutical industry, academic institutions, and individual investigators for the early clinical evaluation of innovative cancer therapies.
- The ETCTN was created to evaluate these therapies using a coordinated, collaborative, and inclusive team-based approach to early phase experimental therapeutic clinical trials.
 - Collaborative approach
 - Reproducible translational science
 - Not only for solid tumors: network of hematological malignancy trials

ETCTN: Lead Academic (12) and Affiliated Organizations (41)

- Clinical sites participate in a **Phase 1 Program** supported by UM1 grants
- **Phase 2 Program** is supported by cooperative agreements as supplements to the existing phase 1 UM1 grants
- Conduct early clinical trials of NCI-IND agents in high priority areas of unmet medical needs
- Integrate preclinical findings using clinical samples for biomarker analysis
- Promote collaboration among institutions and investigators



Leukemia

Lymphocytic

Relapsed or refractory CD19+ precursor B-lymphoblastic

* 10030: MRD-ERASER 1: Randomized Phase 2 Study of the Anti-PD-L1 Antibody Pembrolizumab in Combination with Conventional Intensive Chemotherapy as Frontline Therapy in Patients with Acute Myeloid Leukemia

Myelogenous

Relapsed or refractory AML, myelodysplastic syndrome, or chronic myelomonocytic leukemia

▼ 10026: A Phase 1 Study of Ipiplimab in Combination with Decitabine in Relapsed or Refractory Myelodysplastic Syndrome/Acute Myeloid Leukemia

10247: A Randomized Phase II Trial of MLN4924 (Pevonedistat) with Azacitidine Versus Azacitidine in Adult Relapsed or Refractory Acute Myeloid Leukemia

▼ 10246: A Phase 1 Study of MLN4924 (Pevonedistat) and Belinostat in Relapsed/Refractory Acute Myeloid Leukemia or Myelodysplastic Syndrome

10237: A Phase 1 Study of MLN7243 (TAK-243) for Either Relapsed/Refractory Acute Myeloid Leukemia or Myelodysplastic Syndrome/Chronic Myelomonocytic Leukemia Refractory to Hypomethylating Agents

10273: A Phase I Study of M3814 in Combination with MEC in Patients with Relapsed or Refractory Acute Myeloid Leukemia

10264: The PRIME Trial: PARP Inhibition in IDH Mutant Effectiveness Trial. A Phase II Study of Olaparib in Isocitrate Dehydrogenase (IDH) Mutant Relapsed/Refractory Acute Myeloid Leukemia and Myelodysplastic Syndrome

AML with wild-type p53

10075: A Phase 1B Study of AMG-232 in Combination with Decitabine in Acute Myeloid Leukemia

AML in complete remission

9706: Randomized Phase II Study to Assess the Role of Nivolumab as Single Agent to Eliminate Minimal Residual Disease and Maintain Remission in Acute Myelogenous Leukemia (AML) Patients After Chemotherapy (REMAIN TRIAL)

AML associated with antecedent myeloproliferative disorder

10147: A Phase II Randomized Study of Topotecan/Carboplatin with or Without Veliparib or Placebo in Advanced Myeloproliferative Disorders and CMML

Mutated AML

▼ 10200: A Phase 1b/II Study of the Histone Methyltransferase Inhibitor Pinometostat in Combination with Azacitidine in Patients with 11q23-Rearranged Acute Myeloid Leukemia

* 10317: Checkpoint Blockade to Overcome Resistance in TP53 Mutated Acute Myeloid Leukemia

10212: A Phase 1b/2 Study of Pinometostat in Combination with Standard Induction Chemotherapy in Newly Diagnosed Acute Myeloid Leukemia with MLL Rearrangement

AML (front line therapy)

* 10300: Randomized Phase 2 Study of the Anti-PD-L1 Antibody Pembrolizumab in Combination with Conventional Intensive Chemotherapy as Frontline Therapy in Patients with Acute Myeloid Leukemia

* 10334: Blockade of PD-1 Added to Standard Therapy to Target Measurable Residual Disease in Acute Myeloid Leukemia 2 (BLAST MRD AML-2): A Randomized Phase 2 Study of the Venetoclax, Azacitidine, and Pembrolizumab (VAP) Versus Venetoclax and Azacitidine as Frontline Therapy in Newly Diagnosed Acute Myeloid Leukemia (AML) with IDH1/2 Mutation

Myelodysplastic syndrome

MDS or oligoblastic AML

10009: A Phase 1b Study of the Anti-PD1 Antibody Pembrolizumab in Combination with the Histone Deacetylase Inhibitor, Enlistat for Treatment of Patients with Myelodysplastic Syndromes After DNA Methyltransferase Inhibitor Therapy Failure

Hematologic malignancy

Hematologic malignancy, not otherwise stated

10014: A Pilot Study of Atezolizumab (MPDL3280A) Following Adoptive Cell Transfer in Active Hematologic or Solid Tumor Malignancies

Entinostat and Pembrolizumab in Treating Patients With Myelodysplastic Syndrome After DNMTi Therapy Failure



The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT02936752

[Recruitment Status](#) ⓘ : Recruiting

[First Posted](#) ⓘ : October 18, 2016

[Last Update Posted](#) ⓘ : June 6, 2019

See [Contacts and Locations](#)

Sponsor:

National Cancer Institute (NCI)

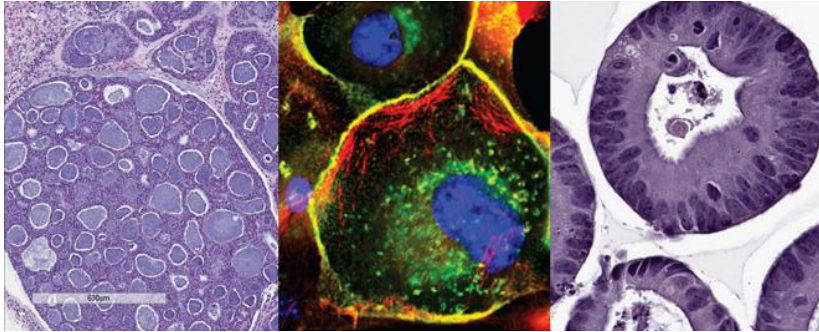
Information provided by (Responsible Party):

National Cancer Institute (NCI)

PDMR



PDMR NCI Patient-Derived Models Repository
An NCI Precision Oncology Initiative™ Resource



<https://pdmr.cancer.gov/>

- Patient-derived xenografts (PDXs), in vitro patient-derived tumor cell cultures (PDCs) and cancer associated fibroblasts (CAFs) as well as patient-derived organoids (PDOrg)
- Clinically-annotated with molecular information available in an easily accessible database
- Develop models allowing comparative assessment of molecular predictors of drug efficacy.
- Establish predictive genomic signatures and/or proof of mechanism pharmacodynamics
- Available to the extramural community

Opportunities

- Current and upcoming trial options for MDS patients
 - Clofarabine+bortezomib
 - Aza-TdC
- DTC participates within ETCTN: trials within this network are available to our clinic
- High priority area for DTC

 [@NCItreatment](https://twitter.com/NCItreatment)
<http://dtc.cancer.gov>



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