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
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 List

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

Tumor Type
- All Cancer Types
- Sarcoma
- Lymphoma
- MDS
- Rare Tumors

Trial Type
- Immunotherapy
- Precision Medicine

Trial Phase
- Phase 1
- Phase 2

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

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

**Figure 1.** Efficacy of Aza-TdC (aza-TdCyd) and TdCyd in human tumor xenograft models.
Experimental Therapeutics
Clinical Trials Network
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
ETCTN Trials by Disease/ Treatment Area: Leukemia

Leukemia

Myelogenous

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

AML with wild-type p53
AML in complete remission
AML associated with antecedent myeloproliferative disorder

Mutated AML

AML (front line therapy)

Myelodysplastic syndrome

MDS or oligoblastic AML

Hematologic malignancy

Hematologic malignancy, not otherwise stated

9033: MRD-ERAS 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

10026: A Phase I Study of Iplimumab 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 MLN4724 (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 Clalaparib in Isocitrate Dehydrogenase (IDH) Mutant Relapsed/Refractory Acute Myeloid Leukemia and Myelodysplastic Syndrome

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

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)

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

10121: A Phase 1b/II Study of the Histone Methyltransferase Inhibitor Phosmobetstat in Combination with Azacitidine in Patients with t(1q23)-Rearranged Acute Myeloid Leukemia

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

10112: A Phase 1b/2 Study of Pinotemostat in Combination with Standard Induction Chemotherapy in Newly Diagnosed Acute Myeloid Leukemia with MLL Rearrangement

10390: 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

10354: Blockade of PD-1 Added to Standard Therapy to Target Measurable Residual Disease in Acute Myeloid Leukemia 2 (BLAST MRD AMI). A Randomized Phase 2 Study of the Vantocatant, Arachidonic Acid, and Pembrolizumab (VAP) versus Venetoclax and Arachidonic acid as Frontline Therapy for Acute Myeloid Leukemia

10509: A Phase 1b Study of the Anti-PD1 Antibody Pembrolizumab in Combination with the Histone Deacetylase Inhibitor Entinostat for Treatment of Patients with Myelodysplastic Syndromes After DNA Methyltransferase Inhibitor Therapy Failure

10414: A Pilot Study of Atezolizumab (MPDL3280A) Following Adoptive Cell Therapy in Active Hematologic or Solid Tumor Malignancies

NOTE: * No ClinicalTrials.gov webpage is available at this time (typically for approved LOIs or protocols in review). ▼ Limited trial; not open ETCTN-wide. Version Date: June 12, 2019
Entinostat and Pembrolizumab in Treating Patients With Myelodysplastic Syndrome After DNMT1 Therapy Failure

ClinicalTrials.gov Identifier: NCT02836752

Recruitment Status: Recruiting
First Posted: October 18, 2016
Last Update Posted: June 6, 2019

See Contacts and Locations

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.

Sponsor:
National Cancer Institute (NCI)

Information provided by (Responsible Party):
National Cancer Institute (NCI)

Open at multiple sites
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

https://pdmr.cancer.gov/
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

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http://dtc.cancer.gov