BIOGRAPHICAL SKETCH

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NAME: DiNardo, Courtney D

eRA COMMONS USER NAME: cdinardo

POSITION TITLE: Associate Professor (Tenure)

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Emory University, Atlanta, GA	BS	6/2002	Biology
University of Michigan, Ann Arbor, MI	MD	6/2006	Medicine
University of Pennsylvania, Philadelphia, PA	Fellowship	6/2012	Hematology/Oncology
University of Pennsylvania, Philadelphia, PA	MSCE	8/2012	Clinical Epidemiology

A. Personal Statement

My primary clinical focus is individualizing therapy and precision oncology in myeloid malignancies, particularly the incorporation of genomics into standard risk assessments and treatment algorithms, and the clinical evaluation of targeted therapeutics within molecularly-defined patient subgroups. I have over 7 years of experience in designing, overseeing, and executing successful clinical trials, from Phase 1 first-in-human dose finding studies to innovative Phase II investigator initiated trials to serving as the international lead of randomized Phase III studies.

My clinical research skills include expertise in trial design through the successful completion of a Master's of Science in Clinical Epidemiology. Through this program I gained invaluable proficiency in epidemiology, biostatistics, trial design, and database management through the timely analysis of IDH mutations, serum 2-hydroxyglutarate (2HG) levels, and clinical outcome in AML patients treated on the ECOG 1900 trial. The hypothesis that IDH mutations contribute to AML pathogenesis through regulation of gene expression via DNA hypermethylation, a process regulated by 2HG, and that 2HG measurement and quantification may become an important therapeutic and minimal residual disease marker, provided the essential groundwork for involvement in the developing evaluation of IDH mutations and IDH therapeutics in AML. This original research laid the groundwork for ongoing involvement in the development, design and execution of several practice-changing trials of novel targeted agents for AML.

I am fortunate to have served as the PI of multiple influential trials involving IDH and BCL2 inhibitors, with comprehensive translational and correlative analyses performed through established collaborations and taking advantage of our comprehensive departmental database, and processing and biospecimen bank. I am honored to have played an integral role in the development and subsequent FDA approval of three agents since 2017: the first-in-class IDH2 inhibitor enasidenib (AG221), the IDH1 inhibitor ivosidenib (AG120), as well as the BCL2 inhibitor venetoclax in combination with hypomethylating agents for newly diagnosed AML.

B. Positions and Employment

2012 – 2018 Assistant Professor, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

2018 – Associate Professor with Tenure, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Credentials:

Board Certification:

2009 - American Board of Internal Medicine
2012 - American Board of Internal Medicine, Hematology
2012 - American Board of Internal Medicine, Oncology

Active Licensures:

2012 - Texas Medical Board, TX, P2851

Other Experience and Professional Memberships

2009 - Member, American Society of Hematology
2009 - Member, American Society of Clinical Oncology
2013 - Member, SWOG Southwest Oncology Group
2016 - Associate Vice Chair, Institutional Review Board, MD Anderson Cancer Center
2016 - Member, Graduate School of Biomedical Sciences, Houston, TX
2017 - Member, MDS/AA Patient Education Counsel
2018 - Member, *Blood* Journal Editorial Board
2018 - Member, ASH Working Group on Innovations in Clinical Trials
2018 – Member of Inherited Heme Malignancy Working Group, PDQ Cancer Genetics Editorial Board
2018 - Member, Clinical Cancer Genetics Steering Committee, MD Anderson Cancer Center

Honors

2004 Alpha Omega Alpha Honor Society, Alpha Omega Alpha
2012 ASCO Young Investigator Award, American Society of Clinical Oncology
2014 R. Lee Clark Fellowship Award, UT MD Anderson Cancer Center
2019 Top Healthcare Performer, scoring in the Top 1% nationally on CAHPS patient experience
2019 The "Best Mentor of the Year" Award, elected by the 2019 MDACC Leukemia Fellows

C. Contribution to Science

1. Development of the Hereditary Hematologic Malignancy Clinic. The HHMC was established in April 2014. This now weekly clinic provides genetic counseling, risk assessment, and clinical and research-based genetic testing for individuals suspected to have inherited predisposition to hematologic malignancy, based on personal and family history as well as distinguishing clinicopathologic characteristics. Experiences and discoveries from this clinic are improving the ability to screen and detect appropriate patients, optimize treatment planning, develop surveillance algorithms for family members, and evaluate preventative approaches.

    a. **DiNardo CD**, Bannon SA, Routbort M, et al. Evaluation of Patients and Families with Concerns for Predispositions to Hematologic Malignancies Within the Hereditary Hematologic Malignancy Clinic (HHMC). Clin Lymphoma Myeloma Leuk 2016 April 27. PMID: 27210295
    b. **DiNardo CD**. Getting a handle on hereditary CEBPA mutations. Blood. 2015 Sep 3;126(10):1156-8. PubMed PMID: 26337351.
    c. Swaminathan M, Bannon SA, Routbort M…**DiNardo CD**. Hematologic malignancies and Li-Fraumeni Syndrome. Cold Spring Harb 2019 Feb 1(5)(1). PMID 30709875
    d. **DiNardo CD**, Routbort MJ, Bannon SA, et al. Improving the Detection of Patients with Inherited Predispositions to Hematologic Malignancies Using Next-Generation Sequencing-Based Leukemia Prognostication Panels. Cancer 2018 Jul 1;124(13):2704-13. PMID: 29682723

2. Clinical Development of Targeted IDH1 and IDH2 inhibitors for patients with IDH1 and IDH2 mutations: The collaborative nature of my early research involving 2HG analysis in IDH mutant AML has opened doors for well-designed clinical trials of IDH1 and IDH2 inhibitors. I am now the PI or Co-PI on numerous ground-breaking IDH-inhibitor as both single agents and rational combinations,

and am leading the international accrual for multicenter sponsored studies as well as running several high impact novel combinations in Phase 1/2 investigator initiated trials.

a. **DiNardo CD**, Stein EM, de Botton S, Roboz GJ, et al. Durable Remissions with Ivosidenib in IDH1-Mutated Relapsed or Refractory AML. NEJM 2018 June 21; 378(25):2386-98, PMID: 29860938
b. **DiNardo CD**, Propert KJ, Loren AW, Paietta E, Sun Z, Levine RL, et al. Serum 2-hydroxyglutarate levels predict isocitrate dehydrogenase mutations and clinical outcome in acute myeloid leukemia. Blood. 2013 Jun 13;121(24):4917-24. PubMed PMID: 23641016; PubMed Central PMCID: PMC3682342.
c. **DiNardo CD**, Jabbour E, Ravandi F, Takahashi K, Daver N, Routbort M, Patel KP, Brandt M, Pierce S, Kantarjian H, Garcia-Manero G. IDH1 and IDH2 mutations in myelodysplastic syndromes and role in disease progression. Leukemia 2015. Jul 31. PubMed PMID 26228814
d. **DiNardo CD**, Ravandi F, Agresta S, Konopleva M, Takahashi K, Kadia T, Routbort M, Patel KP, Mark Brandt, Pierce S, Garcia-Manero G, Cortes J, Kantarjian H. Characteristics, clinical outcome, and prognostic significance of IDH mutations in AML. Am J Hematol. 2015 Aug;90(8):732-6. PubMed PMID: 26016821; PubMed Central PMCID: PMC4612499.

3. Clinical Development of small molecule BCL2 inhibition in AML: The effectiveness of the BCL2 selective inhibitor venetoclax in combination with hypomethylating agent therapy or low-dose cytarabine has changed the landscape of AML therapy nearly overnight. These combinations have quickly become standard of care for older AML patients, and the evaluation of venetoclax with other combination approaches for younger AML patients and relapsed/refractory patients are ongoing in our current clinical trials. I have been fortunate to serve as the lead collaborative PI for the original Phase 1 study of HMA + Venetoclax which led to the accelerated FDA approval of this important treatment regimen.
   a. **DiNardo CD**, Pratz K, Pullarkat V, Jonas BA, Arellano M, et al. Venetoclax Combined with Decitabine or Azacitidine in Treatment-Naïve, Elderly Patients with Acute Myeloid Leukemia. Blood 2019; 133(1):7-17. PMID: 6318429
   b. **DiNardo CD**, Perl AE. Advances in patient care through increasingly individualized therapy. Nat Rev Clin Oncol 2019; 16(2):73-74. PMID: 30602758
   c. **DiNardo CD** , Pratz KW , Letai A, Jonas BA, Wei AH, Thirman M, Arellano M, Frattini MG, Kantarjian H, Popovic R, Chyla B, Xu T, Dunbar M, Agarwal SK, Humerickhouse R, Mabry M, Potluri J, Konopleva M, Pollyea DA. Safety and preliminary efficacy of venetoclax with decitabine or azacitidine in elderly patients with previously untreated acute myeloid leukaemia: a non-randomised, open-label, phase 1b study. Lancet Oncol, 1/2018. PMID: 29339097.
   d. Agarwal SK, **DiNardo CD**, Potluri J, Dunbar M, Kantarjian HM, Humerickhouse RA, Wong SL, Menon RM, Konopleva MY, Salem AH. Management of Venetoclax-Posaconazole Interaction in Acute Myeloid Leukemia Patients: Evaluation of Dose Adjustments. Clin Ther 2017 39(2)359-367. PMID: 28161120

4. Glutaminase inhibition in myeloid malignancies: Given expertise in this expanding field of AML cancer metabolomics, I am co-Investigator on the R01 (PI: Marina Konopleva) “Therapeutic targeting of glutamine metabolism in MDS”. The goal of this research project is to investigate the therapeutic targeting of glutamine metabolism in myelodysplastic syndromes. Specifically, we will evaluate whether CB-839, an oral glutaminase inhibitor, is effective in combination with hypomethylating agent therapy for the treatment of high-risk myelodysplastic syndromes, within a Phase I/II investigator-initiated study where I serve as the PI of the ongoing clinical trial.
   a. Matre P, Shariati M, Velez J, Qi Y, Konoplev S, Su X, **DiNardo CD**, Daver N, Majeti R, Andreeff M, Chan SM, Konopleva M. Inhibiting glutaminase in AML: metabolic dependency of selected AML subtypes. Oncotarget 2016; 7(48):79722-735. PMID: 5340236
   b. Guerra V, Burger JA, Borthakur G….Konopleva M, **DiNardo CD**. Interim analysis of a Phase II Study of the Glutaminase Inhibitor Telaglenastat (CB-839) in Combination with Azacitidine in Advanced MDS. Blood 12/2019, Abstract #567

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

12716 DiNardo (PI) 10/3/2014-present
Daiichi-Sankyo
2014-0565: A Phase 1 Dose Escalation Study of DS-3032B, an Oral MDM2 Inhibitor, in Subjects with Acute Myelogenous Leukemia (AML), Acute Lymphocytic Leukemia (ALL), Chronic Mylogenous Leukemia (CML) in Blast Phase, or High-Risk Myelodysplastic Syndrome
Study safety and efficacy of DS-3032B in AML, ALL, CML-Blast Phase, or High-Risk MDS.
Role: Principal Investigator

1 R01 CA206210-01 Konopleva (PI) 4/1/2016-3/31/2021
NIH/NCI
Therapeutic targeting of glutamine metabolism in MDS
Study the efficacy and mechanisms of action of CB-839 in pre-clinical MDS models and in a human clinical trial.
Role: Co-Investigator

51584 DiNardo (PI) 5/19/2016-present
Celgene Corporation
2015-0781: A Phase 3, Multicenter, Open-label, Randomized Study Comparing the Efficacy and Safety of AG221 (CC-9007) versus Conventional Regimens in Older Subjects with Late Stage Acute Myeloid Leukemia Harboring an Isocitrated Dehydrogenase 2 Mutation
To determine the primary efficacy, measured as overall survival (OS), of AG-221 compared with conventional care regimens (CCRs) in subjects 60 years or older with AML refractory to or relapsed after second- or third-line AML therapy and positive for an IDH2 mutation.
Role: Principal Investigator

54049 DiNardo (PI) 6/5/2017-6/4/2020
Bayer
2016-1084: An open-label, non-randomized, multicenter Phase I study to determine the maximum tolerated and / or recommended Phase II dose of oral mutant IDH1 (mIDH1) inhibitor BAY 1436032 and to characterize its safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary clinical efficacy in patients with mIDH1-R132X advanced acute myeloid leukemia (AML)
Determine the safety, tolerability, maximum tolerated dose (MTD) and/or recommended Phase II dose (RP2D) of BAY 1436032 in a 2 times daily (BID) dosing schedule in patients with mutant IDH1 (mIDH1) R132X advanced AML
Role: Principal Investigator

DiNardo (PI) 8/1/2017-1/31/2020
MD Anderson MEBRS and HI-CRSP Funding Support
2016-0636: Phase Ib/II study of the glutaminase inhibitor CB-839 in combination with azacitidine in subjects with advanced myelodysplastic syndrome
assessment of the safety, tolerability and efficacy of the glutaminase inhibitor CB-839 in combination with azacitidine (AZA) for the treatment of advanced MDS.
Role: Principal Investigator

53895 DiNardo (PI) 9/29/2017-12/31/2020
Abbvie
2016-0985: A Randomized, Double-Blind, Placebo Controlled Study of Venetoclax in Combination with Azacitidine Versus Azacitidine in Treatment Naïve Subjects with Acute Myeloid Leukemia Who Are Ineligible for Standard Induction Therapy
To evaluate if venetoclax in combination with azacitidine will improve overall survival (OS) and composite complete remission rate (complete remission + complete remission with incomplete marrow recovery; CR + CRi) versus placebo in combination with azacitidine, in treatment naïve subjects with acute myeloid leukemia (AML).
Role: Principal Investigator

DiNardo (PI) 10/1/2017-9/30/2019
MD Anderson's Khalifa Scholar Award
Study of the IDH1-mutant inhibitor ivosidenib with the BCL2-inhibitor venetoclax in IDH1-mutated AML
To conduct the first rational combination of IDH1 inhibition, in combination with oral small molecule BCL2-inhibition.
Role: Principal Investigator

DiNardo (PI) 11/1/2017-10/31/2020
UT MD Anderson Cancer Center
Study of the IDH1-mutant inhibitor ivosidenib with the BCL2-inhibitor venetoclax in IDH1-mutated AML
To provide a detailed mechanistic understanding of both metabolic and genomic patterns of response and resistance with the combination of IDH1 inhibition with oral small molecule BCL2-inhibition.
Role: Principal Investigator

DiNardo (PI) 1/1/2018-12/31/2020
V Foundation/Lloyd Family Clinical Oncology Scholar Award
A comprehensive clinical trial program for patients with IDH mutations
To successfully implement and complete several investigator-initiated, hypothesis-driven clinical trials at MD Anderson for patients with IDH-mutated myeloid malignancies.
Role: Principal Investigator

2018-0556 DiNardo (PI) 9/18/2018-9/17/2025
Clear Creek Bio, Inc
2018-0556: A Phase 1b/2a Open-Label, Multi-Center Study to Assess the Safety, Efficacy and Pharmacokinetics of Intrapatient Dose-Adjusted Brequinar and Inhibition of Dihydroorotate Dehydrogenase (DHODH) in Adult Subjects with Acute Myelogenous Leukemia (AML)
Role: Principal Investigator

Completed Research Support

2-P50-CA-100632-16 DiNardo (PI) 9/1/2018-8/31/2019
NIH/NCI
Improving the recognition, treatment, and prevention strategies for patients with inherited predispositions to hematologic malignancies
improve upon the accurate identification of patients and families with hereditary hematologic malignancies, and (2) utilize genomic and transcriptomic sequencing evaluations to improve screening and surveillance approaches, tailor treatment decisions, and ultimately develop customized prevention strategies for patients and families with hereditary hematologic cancer syndromes
Role: Principal Investigator