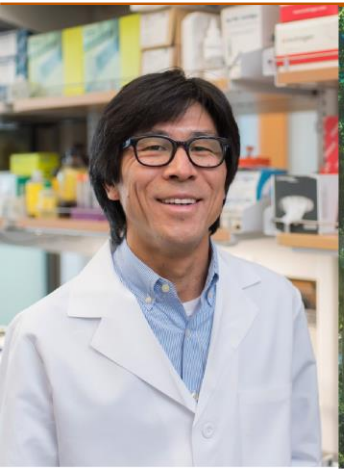
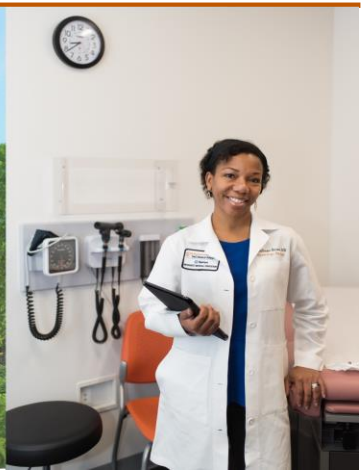
The University of Texas at Austin
Dell Medical School

LIVESTRONG CANCER INSTITUTES





CPRIT Clinical Trials Advisory Committee Fiscal Year 2023 Annual Report

CPRIT Oversight Committee Meeting
August 16, 2023
S. Gail Eckhardt M.D.

CTAC Membership: Expanded

- **S. Gail Eckhardt, MD**, Livestrong Cancer Institute, DMC, UT Austin
- **Carlos Arteaga, MD**, Harold Simmons Comprehensive Cancer Center, UTSWMC
- **Ruma Bhagat MD, MPH**, Genentech, Inc.
- **Suzanne Cole, MD, FACP, FASCO**, Community Oncology Program UTSWMC
- **David Gerber, MD,** Clinical Cancer Research, UTSWMC
- **David S. Hong, MD**, UTMDACC
- **Ronan Kelly, MD,** Baylor Scott and White
- **Pavan Reddy, MD**, Director, Dan L Duncan Comprehensive Cancer Center, Baylor College of Medicine
- **C. Patrick Reynolds, MD, PhD,** Cancer Center, TTUHSC

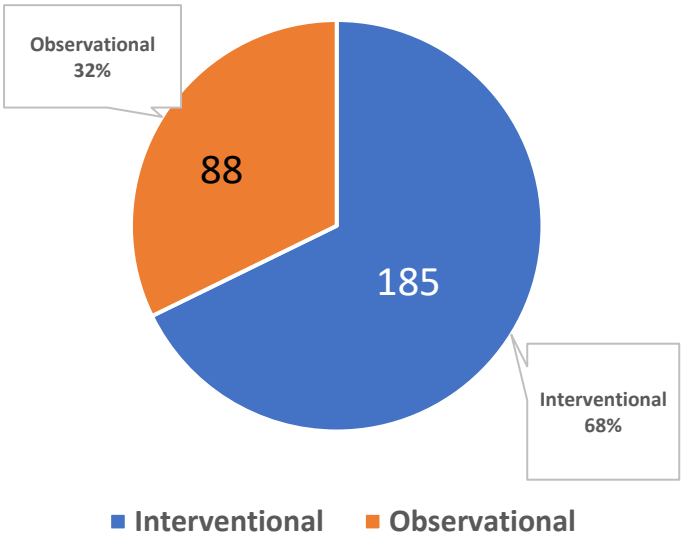
Completed 2022 CTAC Goals

1. Membership Expansion:
    - Added new Director of the Dan Duncan Comprehensive Cancer Center, Baylor College of Medicine
    - Added a Community Oncologist and a Community Clinical Researcher/Trialist members
    - Added an industry member with expertise in engaging diverse communities as well as regulatory knowledge of telehealth, consenting and local labs in early clinical trials
2. Dr. Pat LoRusso (Yale/expertise in early clinical trials and underserved populations) was a CTAC guest speaker and discussed lessons learned from her recently launched *"hybrid decentralization model"*—mechanism to expand trials to community sites
3. Dr. Beg, Vice President, Oncology for *Science 37* presented an overview of services they provide to expand access to clinical trials globally via a centralized digital platform

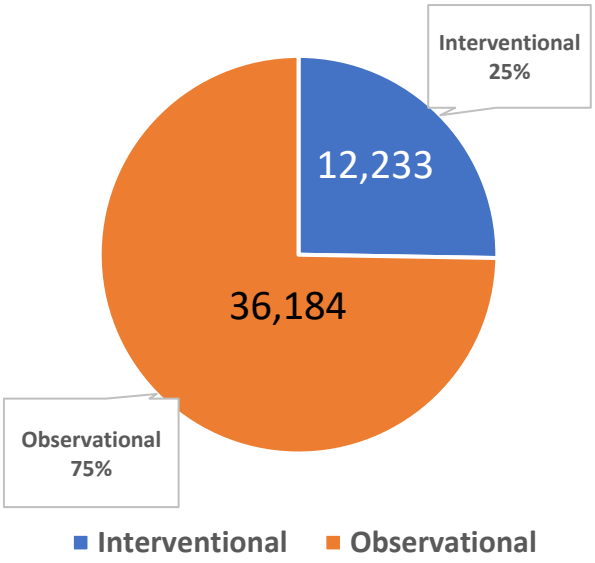
Cumulative Clinical Research Data

CPRIT Research Programs: 273 clinical trials; **48,417** patients enrolled; **8258** publications

Clinical Trials by Type of Trial



Patients Enrolled by Type of Trial



CTAC Recommendations to CPRIT

1. **Continue to refine the CTNA RFA to ensure we are diversifying the spectrum of patients enrolled in clinical trials across Texas**
   - Including rural patients
   - Utilize telehealth
2. **Consider partnering with NCI/CTEP on developing new initiatives that can be launched in Texas**
3. **Potential new RFAs to consider:**
   - K24-like mechanism to provide support for mentors (RFA for new Clinical Investigator Award)
   - Grand Challenge-like Awards
   - SU2C Catalyst-like awards
4. **Initiate regular meetings of cancer center leadership with rotating venue to discuss recruitment awards and new initiatives**

A Phase II, Multicenter, Prospective Study of Sacituzumab Govitecan in Recurrent Glioblastoma

Presented by William Kelly MD

Mays Cancer Center

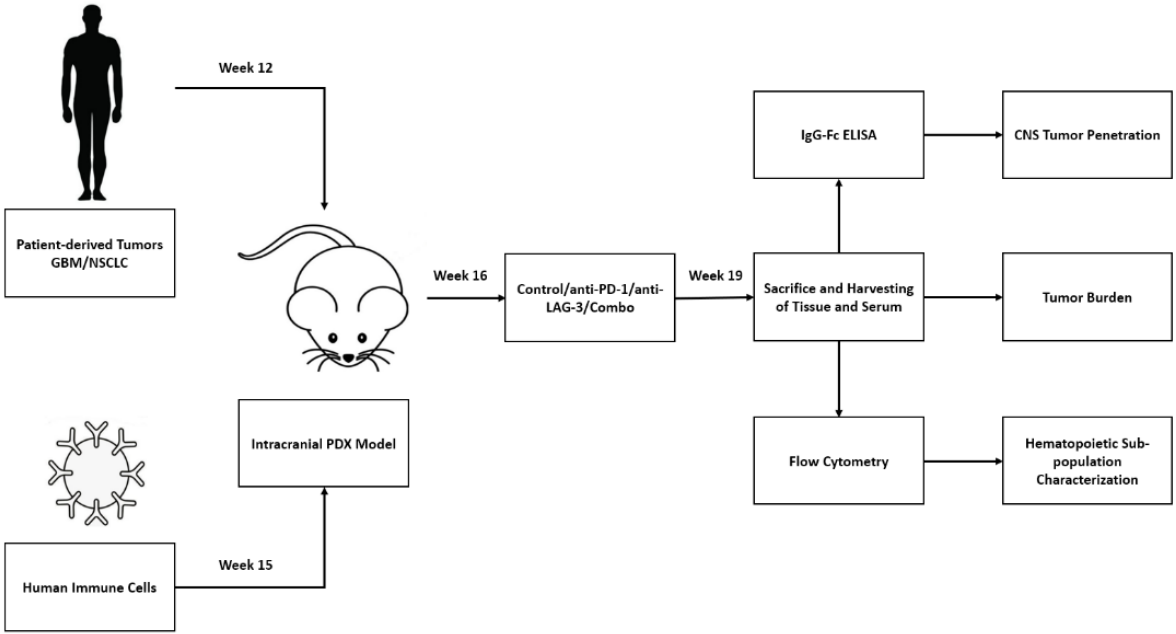
Disclosures: I have no personal, professional or financial relationships that would constitute a conflict of interest.

Clinical Research

- Principal Investigator for 'A Phase II, Multicenter, Prospective Study of Sacituzumab Govitecan in Recurrent Glioblastoma' (NCT04559230). Recruiting 12/9/21.
- Principal Investigator for 'A Phase II, Investigator-initiated Study of Imipramine Hydrochloride and Lomustine in Recurrent Glioblastoma' (NCT04863950). Recruiting 11/5/21.
- Principal Site Investigator for 'A Phase II, Open-label, Multicenter Study Evaluating the Safety and Efficacy of Neoadjuvant and Adjuvant Tiragolumab Plus Atezolizumab, with or without Platinum-based Chemotherapy, in Patients with Previously Untreated Locally Advanced Resectable Stage II, IIIA or Select IIIB Non-small Cell Lung Cancer' (NCT04832854). Recruiting 7/28/23.
- Principal Site Investigator for 'Phase II Trial of SMO/AKT/NF2/CDK Inhibitors in Progressive Meningiomas with SMO/AKT/NF2/CDK Pathway Mutations' (NCT02523014). Recruiting 11/3/22.

Basic Science Research

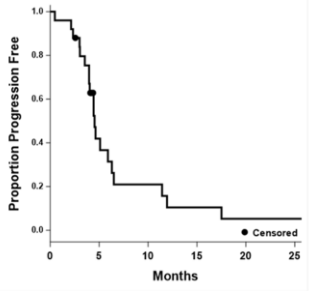
- PDX Model of PD-1 and LAG-3 Blockade in Glioma. Relatlimab and Nivolumab obtained from BMS 12/13/22. Awaiting IACUC protocol.



Recent Peer Reviewed Publications

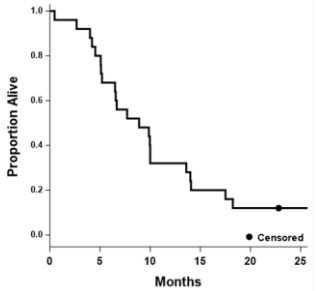
- **Kelly WJ**, Diaz Duque AE, Michalek J, Konkel B, Caflish L, Chen Y, Pathuri SC, Madhusudanannair-Kunnuparampil V, Floyd J, Brenner A. Phase II Investigation of TVB-2640 with Bevacizumab in Patients with First Relapse of High-Grade Astrocytoma. Clin Cancer Res. 2023 Jul 5;29(13):2419-2425.
- Tripathy S, Alvarez N, Jaiswal S, Williams R, Al-Khadimi M, Hackman S, Phillips W, Kaur S, Cervantez S, **Kelly W**, Taverna J. Hypermetabolic Lymphadenopathy Following the Administration of COVID-19 Vaccine and Immunotherapy in a Lung Cancer Patient. J Med Case Rep 2022 Nov 25;16(1):445.
- Kapoor V, **Kelly WJ**. Biomarkers for Immune Checkpoint Inhibitors in Solid Tumors. Clin Transl Oncol. 2022 Sep 14.

Figure 1



Kaplan-Meier Estimate of Progression (All patients, N=25), median=4.5, 95% CI 4.0, 6.3

Figure 2



Kaplan-Meier Estimate of Overall Survival (All patients, N=25) Median=8.9 95% CI 5.2, 13.6

Manuscripts in Progress

- **Kelly WJ**, Balinda H, Michalek J, Surapaneni, P, Floyd J, Brenner A. A Phase 0 Clinical Trial of Sacituzumab Govitecan in Patients with Breast Cancer Brain Metastases and Recurrent Glioblastoma. Manuscript preparation.
- **Kelly WJ**, Gruslova A, Ricardo R, Brenner A. VB-1111 Modulates Macrophage-specific Cytokines in Glioblastoma. In progress.

Abstract Presentations

- **Kelly W**, Balinda H, Ghamasaee P, Gilbert A, Michalek J, Surapaneni P, Floyd J, Brenner A. Sacituzumab Govitecan for Recurrent Glioblastoma. Accepted for presentation by William Kelly at the Society for NeuroOncology Annual Meeting 11/15/23.
- Ghamasaee P, Balinda H, **Kelly W**, Gruslova A, Floyd J, Chiou J, Lodi A, Tiziani S, Brenner A. A Phase 0 Clinical Trial of Sacituzumab Govitecan in Patients with Breast Cancer Brain Metastases. Presented by Henriette Balinda at the San Antonio Breast Cancer Symposium 12/7/22.

Career Development

Academic Performance and Mentorship

- Master of Science in Clinical Investigation and Translational Science Program. 15/30 credits earned to date
- Weekly lab meetings and mentoring with Dr. Brenner

Seminars and Journal Clubs

- Spotlight on Research Integrity 5/24/22
- Thoracic tumor board, neuro-oncology tumor board, grand rounds
- Brenner Lab Journal Club: Bimonthly attendance, presented 5/20/22

Contributions to Scientific Review

- Member of DoD CDRMP Peer Review Panel for Brain Tumors 11/3/22-11/4/22
- Review Editor for Frontiers in Oncology since 7/14/23
- Peer review for Clinical Translational Oncology, Cancer Immunology and Targeted Oncology

Career Development

Teaching

- Monthly didactic lectures to neurology residents and fellows
- Four chemotherapy lectures to medical students per year

Quality Improvement

- QI Project with Dr. Salazar and Student Nurse Practitioner Martinez. 'Reducing Anxiety in Medical Oncology Patients via a Mindfulness Approach'. Presented by April Martinez at the 26th Annual Oncology Symposium by the Association of Physician Assistants in Oncology 8/24/23. First Place Winner.

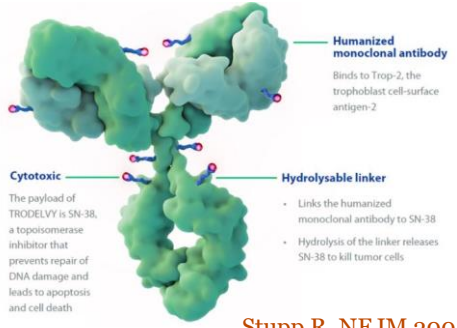
Leadership

- Neuro-Oncology CDST Leader

Background

- Glioblastoma is the most common and aggressive primary malignant brain tumor
- Standard of care is surgery followed by radiation with concurrent and adjuvant TMZ
  - OS of ~14 months
- There are no systemic therapies with proven survival benefit in the recurrent setting
- Trop2 is a transmembrane glycoprotein that participates in calcium signaling
- In glioma, Trop2 expression is highly expressed (95%) but not normal brain tissue
  - This expression correlates with grade, proliferation rate, microvessel density and worsened survival
- Sacituzumab Govitecan is an ADC that is FDA approved in mUC and mTNBC
  - Anti-Trop2 antibody
  - Ph-dependent cleavage site (CL2A)
  - Topoisomerase I inhibitor (SN38)

rGBM: Recurrent Glioblastoma
TMZ: Temozolomide
OS: Overall Survival
Trop2: Trophoblast cell-surface antigen 2 (TACSTD2)
ADC: Antibody-drug conjugates
mUC: Metastatic Urothelial Cancer
mTNBC: Metastatic Triple Negative Breast Cancer

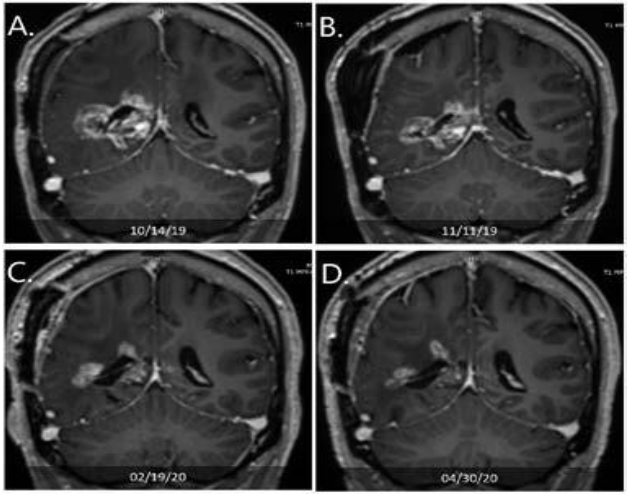


Stupp R, NEJM 2005.
Ning S, Neurol Sci 2013.

Background

- We initiated a single center, prospective, window-of-opportunity trial of 10 patients with rGBM and 11 breast cancer patients with BM
  - Administered single dose SG (10mg/kg IV) on D-1 of surgery
  - Undergo elective craniotomy with intraoperative tumor and serum collection
  - Continued on SG D1 and 8 q21 days
  - Among first 14 patients 2 PR were observed
  - Among sufficient rGBM samples, SN-38 tissue concentrations varied from 39.7 nM to 259.1 nM/g (median 176.85 nM/g)

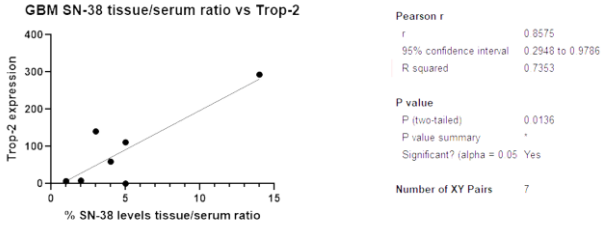
SG: Sacituzumab Govitecan

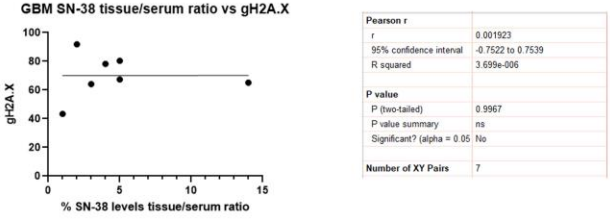


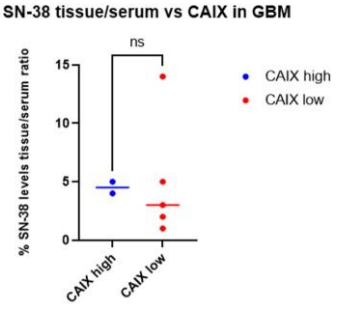
Brenner AJ, Cancer Res 2021.

Background

- As expected, Trop-2 expression correlates with % SN-38 tissue/serum ratio indicating deliver of payload by antibody
- γ-H2AX, a surrogate marker of DNA damage, did not correlate with % SN-38 tissue/serum ratio
  - This had been looked at as a marker of direct deliver
  - However, a lack of correlation could be explained by prior alkylating therapy causing high levels of preexisting DNA damage or a failure of the SN-38 to sufficiently impact DNA in the 1 day interval between dosing and surgery
- CAIX, a surrogate marker of intratumoral hypoxia, did not correlate with % SN-38 tissue/serum ratio, suggesting hypoxia does not appreciably drive indirect SN-38 release







γ-H2AX: Gamma H2A histone family member X
CAIX : Carbonic anhydrase IX

Design

- Multicenter, open-label, single-arm therapeutic trial
  - Mays Cancer Center at UT Health San Antonio
  - Texas Oncology Austin
  - Cleveland Clinic Cancer Center
- Sacituzumab Govitecan 10mg/kg IV, D1 and D8 q21 days

IDHwt: Isocitrate dehydrogenase wild-type

Hypothesis

- That treatment with SG will improve PFS in patients with IDHwt rGBM as compared with a historical control of lomustine monotherapy (EORTC 26101)

Two-stage phase II Bayesian Adaptive Design

- Initial phase
  - Assuming PFS6 with unfavorable and favorable probabilities of 0.17 and 0.34 respectively
  - Assuming posterior probability of 0.95 as threshold for efficacy and 5% cutoff of the predictive probability to stop the trial
  - Interim analysis with trial stopped for futility if ≤2 responses
  - Calculate n=20

Wick W, NEJM 2017

Exploratory Studies

- **Hypoxia via oxygen-enhanced MRI**
  - Collaborative effort with University of Manchester
  - Measures longitudinal relaxation rates (R_{1air}, R_{1O2}) to classify voxels as oxygen enhancing or refractory to oxygen challenge
- **Metabolic Analysis**
  - Collaborative effort with UT Austin
  - Polar metabolites will be analyzed using UHPLC-MS and NMR
  - Fatty acids will be analyzed by GC-MS
  - Complex lipids will be characterized by shotgun lipidomics in conjunction with direct infusion MS

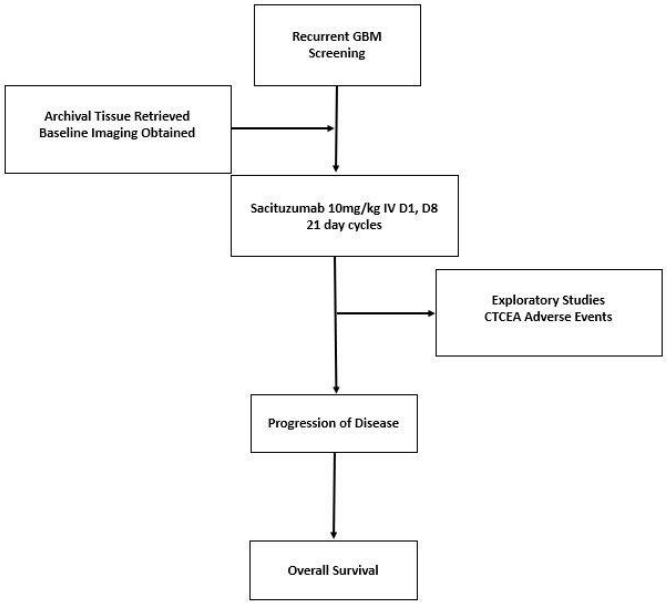
UHPLC-MS: Ultra-high Performance Liquid Chromatography-Mass Spectrometry

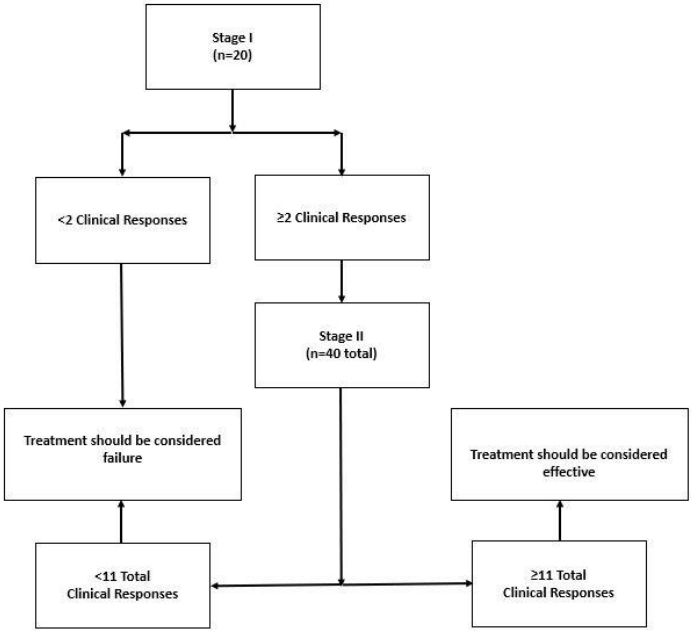
GC-MS: Gas Chromatography-Mass Spectrometry

NMR: Nuclear Magnetic Resonance

CTMS #20-0102

Mays Cancer Center





Thank You

Clinical Trials Network Award (RP220542)

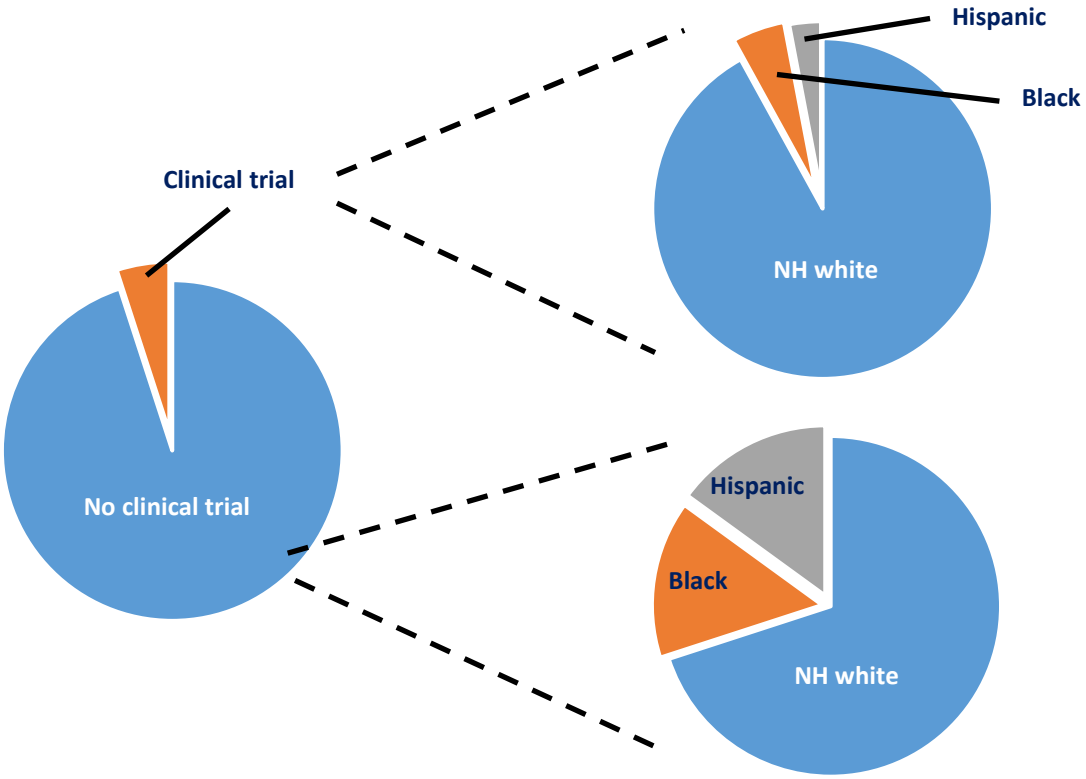
Clinical Trials Participation Award (RP210115)

David E. Gerber, MD
Professor, Department of Internal Medicine and O'Donnell School of Public Health
Harold C. Simmons Comprehensive Cancer Center
UT Southwestern Medical Center
Dallas, Texas

CPRIT Oversight Committee
August 16, 2023

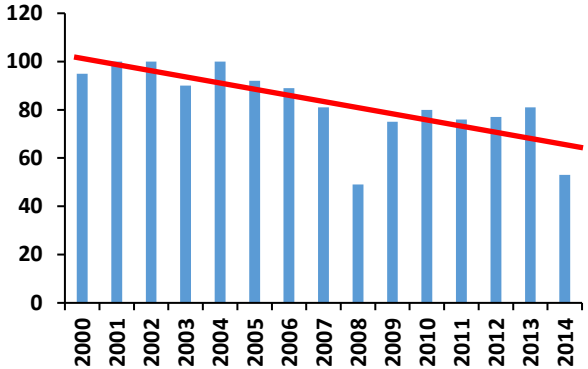
CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

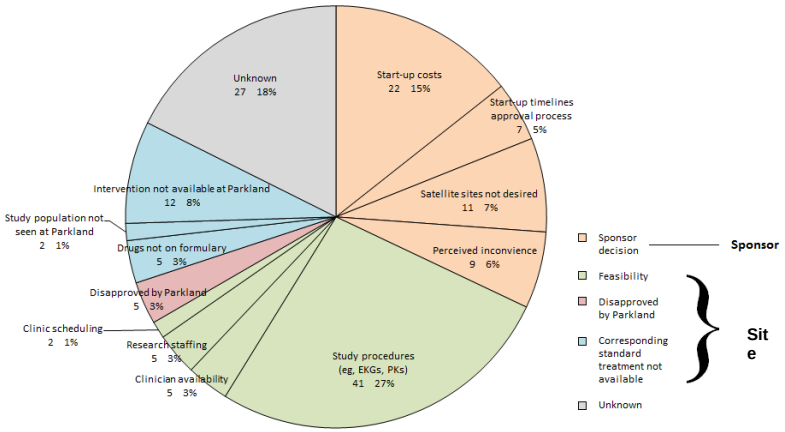
These efforts address a persistent challenges and disparities in accessing cancer clinical trials



Over time, it has become more difficult to offer cancer clinical trials at many clinical sites

A declining proportion of trials in our cancer center could be open at the safety-net clinical site





Diverse reasons underlie this trend

Gerber DE et al. *Oncologist* 2015;20:674-82.

CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

The Texas Clinical Trials Network offers sponsors access to diverse settings and populations

North-Central Texas

Lead institution:

UT Southwestern (Dallas)

Affiliates:

John Peter Smith (Fort Worth)*

Baylor-Scott & White (Temple)

Southeast Texas

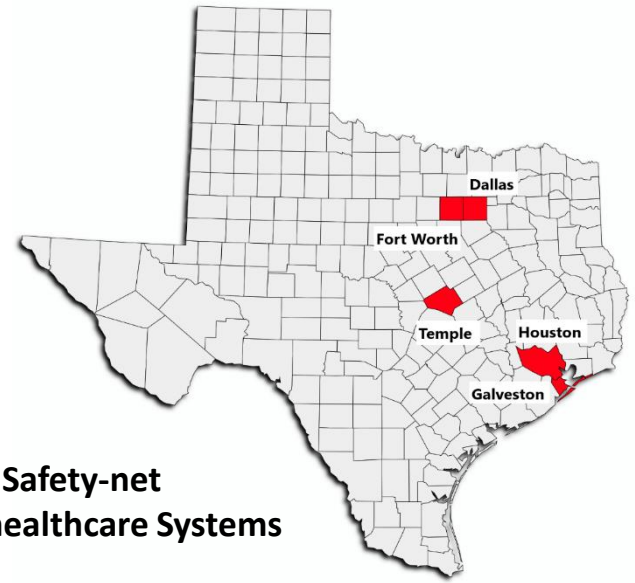
Lead institution:

MD Anderson (Houston)

Affiliates:

Lyndon B. Johnson (Houston)*

UT Medical Branch (Galveston)



***Safety-net healthcare Systems**

CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

The Network is designed to optimize the activation, conduct, and oversight of clinical trials

- CPRIT-supported infrastructure/personnel enhance sites' capabilities
- Critical review of protocols to match sites' populations and needs
- IRB reliance (within regions) to expedite activation
- Shared strategies to enhance awareness of and enrollment to activated trials
- Oversight and *bidirectional* education to support protocol management, data collection, and other trial activities
- Future growth into additional regions of Texas

We introduced the Texas CTNA to clinical trial sponsors in a May 2023 webinar

67 organizations invited

27 organizations attended
- 24 pharma companies
- 3 CROs†

14 organizations have followed up‡
- 12 pharma companies
- 2 CROs

7 trials forwarded for possible activation

Areas of interest / points of clarification
- prioritized phase of trials
- use of central IRB
- consideration of non-therapeutic trials
- potential use of shared contract templates
- future expansion to non-covered regions of Texas
- capacity for hematologic malignancy trials
- time to trial activation
- specific tumor-type expertise within individual Network sites
- planned evaluation measures and intervals
- suggested steps for interested sponsors

†Contract research organizations

‡Including two in-person visits

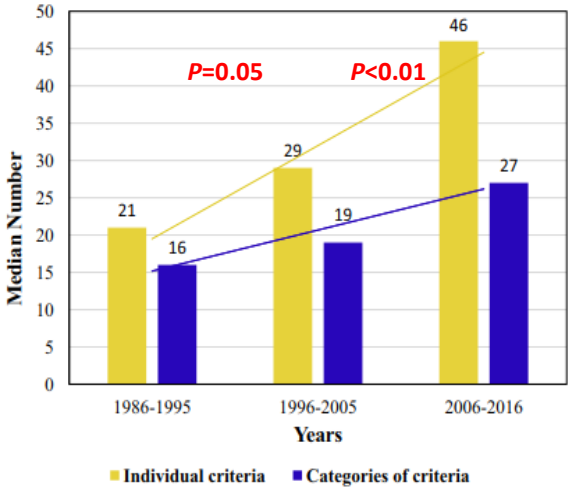
Ultimately, successful enrollment to cancer clinical trials requires clinician and institutional interest and support

How medical oncology trainees benefit from enrolling patients on clinical trials

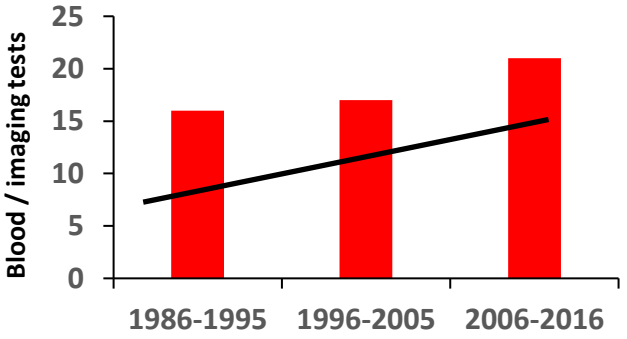
- Skills learned: RECIST, CTCAE, etc
- Authorship opportunities
- Opportunities to participate in related research: secondary data analyses, correlative studies
- Experience valued for multiple future research paths: private practice, academics, industry, regulatory
- Gain experience with new/experimental therapies

Cancer clinical trials add to the substantial burden of standard cancer therapy

Ongoing increase in eligibility criteria



Ongoing increase in screening procedures



Garcia S et al. *J Thorac Oncol* 2017;12:1489-95.

The CTPA provides reimbursement of out-of-pocket costs associated with more frequent (and possibly more distant) travel

Program reimbursement rates.

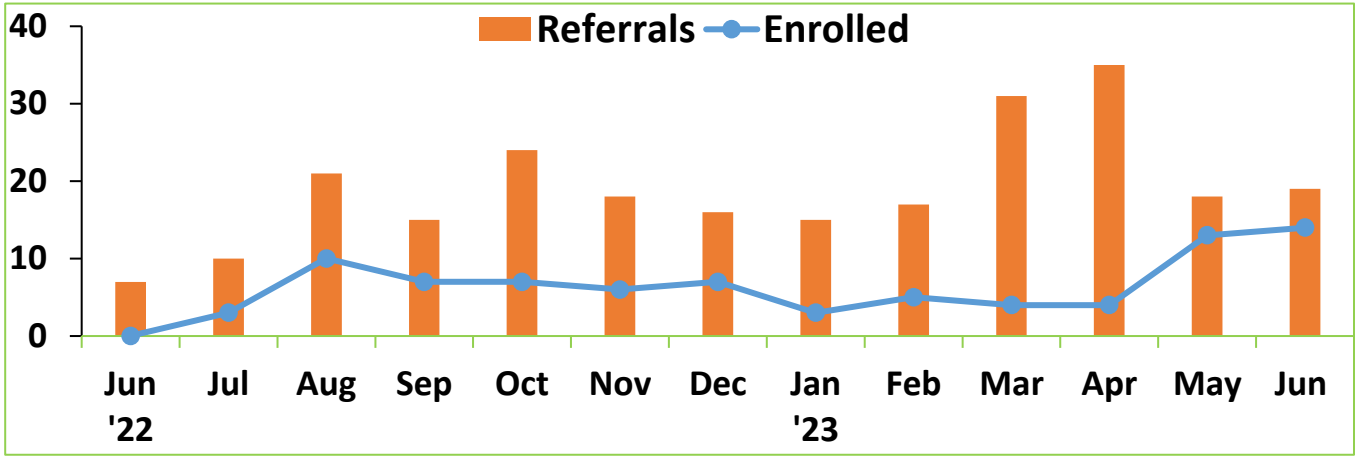
Number in household	Income 0–400%	Income 401%–550%	Income 551% - 700%
1	<$51,040	$51,041 - $70,180	$70,181 - $89,320
2	<$68,960	$68,961 - $94,820	$94,821 - $120,680
3	<$86,880	$86,881 - $119,460	$119,461 - $152,040
4	<$104,800	$104,801- $144,100	$144,101 - $183,400
5	<$122,720	$122,721- $168,740	$168,741 - $214,760
6	<$140,640	$140,641 - $193,380	$193,381 - $246,120
7	<$158,560	$158,561 - $218,020	$218,021 - $277,480
8	<$176,480	$176,481- $242,660	$242,661 - $308,840
REIMBURSEMENT RATE:	100%	75%	50%

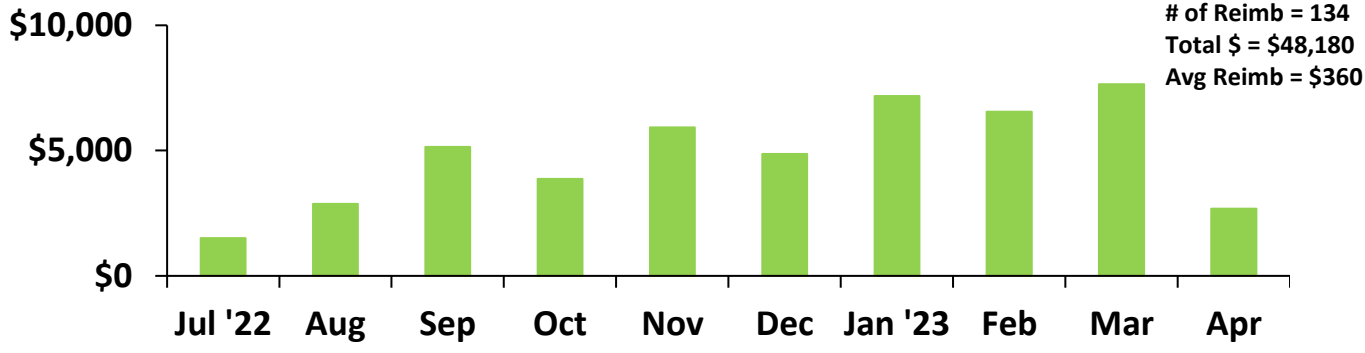
- **Travel**
- **Lodging**
- **Food**
- **Childcare***
  *Depends on available documentation
- **Internet (for telehealth encounters)**

NOT considered inducement or coercion:

- Texas Health & Safety Code, Section 50.0005
- U.S. FDA, “Payment and reimbursement to study subjects” (January 2018)

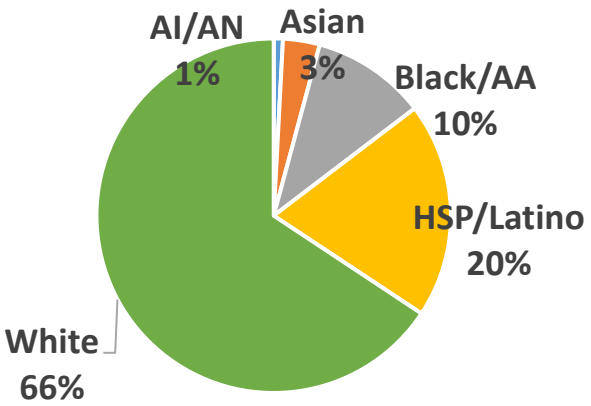
We have been enrolling patients and providing reimbursements for one year



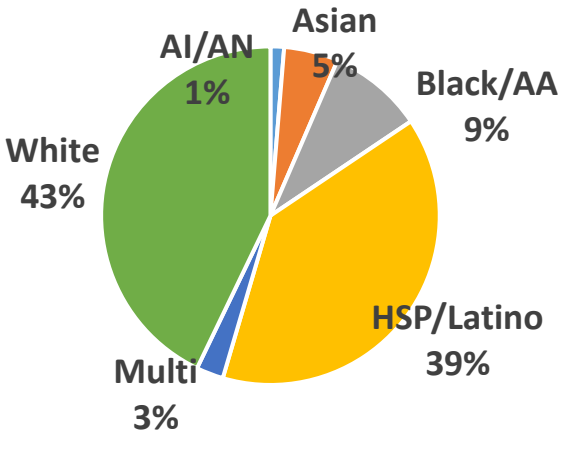


Demographic differences between referred and enrolled populations reveal potential process improvements

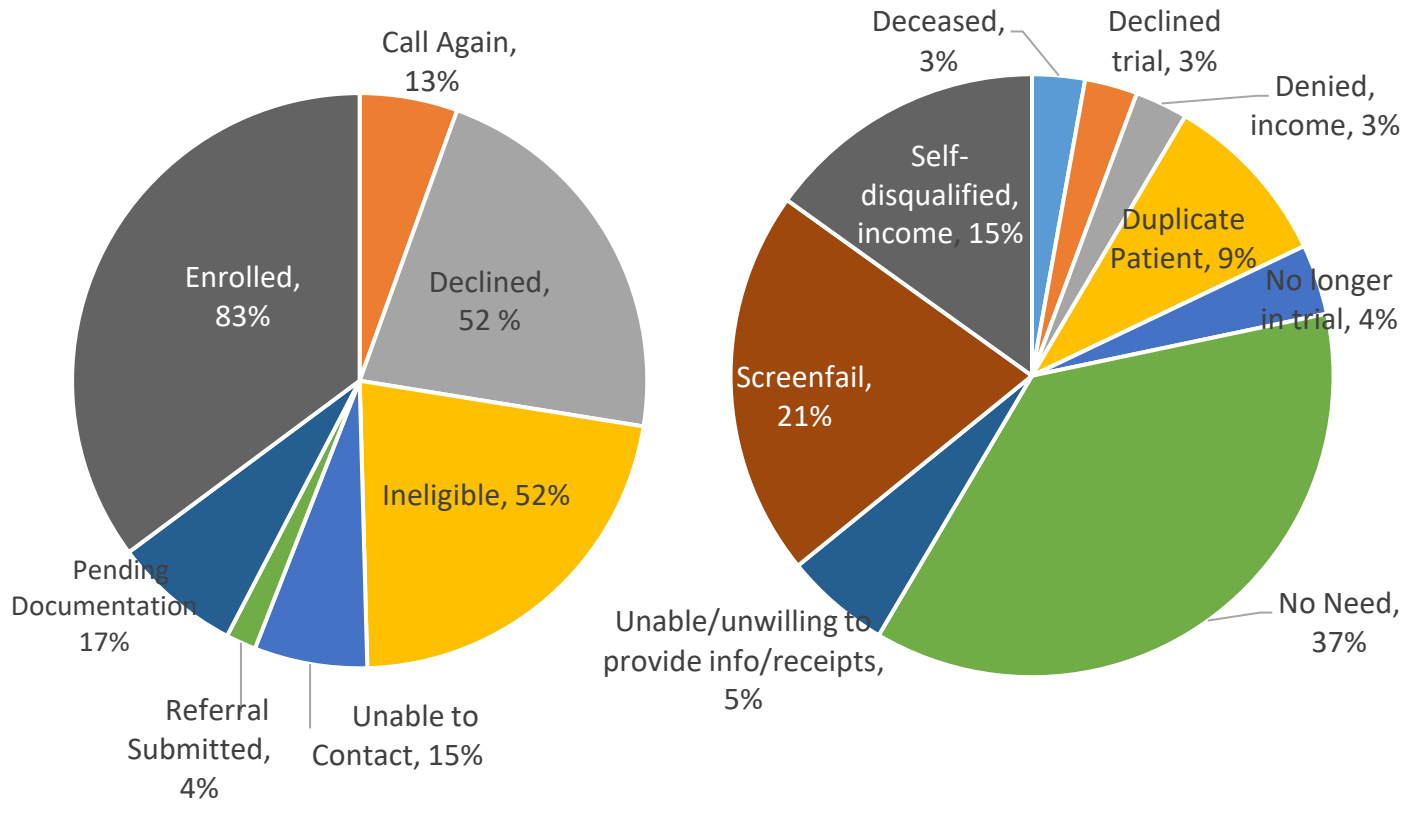
Referred



Enrolled



There are multiple reasons for referred patients not being enrolled in the financial reimbursement program



The CTNA and CTPA are designed to make clinical trials more accessible, equitable, and generalizable

- **The Texas Clinical Trials Network will make cancer clinical trials more accessible to the 30 million diverse residents of Texas**
- **Future growth planned toward the Panhandle and West Texas**
- **Understanding the needs of patients, clinical sites, and study sponsors is critical to trial selection and program success**
- **Assisting patients with out-of-pocket expenses may overcome barriers to clinical trial enrollment and retention**
- **Evaluation of both programs ongoing**

Thank you!