IOWA HEALTH CARE | Holden Comprehensive Cancer Center

Clinical Research

Muhammad Furqan, Interim Associate Director of Clinical Research

EAB MEETING
April 2, 2025

NCI Designated Comprehensive Cancer Center

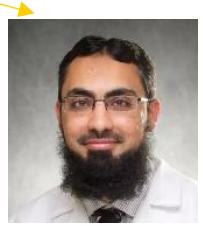
CHANGING MEDICINE.
CHANGING LIVES.®

Overview

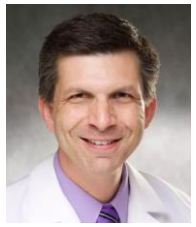
- **Clinical Protocol and Data Management**
- **Protocol Review and Monitoring System**
- **Inclusion in Clinical Research**

Team Structure

Protocol Review & Monitoring Committee (PRMC) Chair
Michael Goodheart, MD



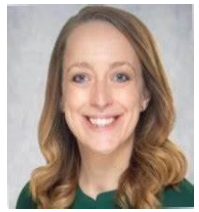
Associate Director, Clinical Research (Interim)
Muhammad Furqan, MD



Data Safety and Monitoring Committee (DSMC) Chair
Doug Laux, MD, MS

Clinical Research Services (CRS) Director
Umar Farooq, MD

Operations Director, Clinical and Translational Research
Kristen Coleman, PhD



Assistant Director, Compliance and Informatics
Cena Jones-Bitterman, MPP, CIP, CCRP

Quality Assurance Officer
Mary Schall, BSN, RN

Assistant Director, Navigation and Network Operations
Mimi McKay, MPH, BSN, CCRP

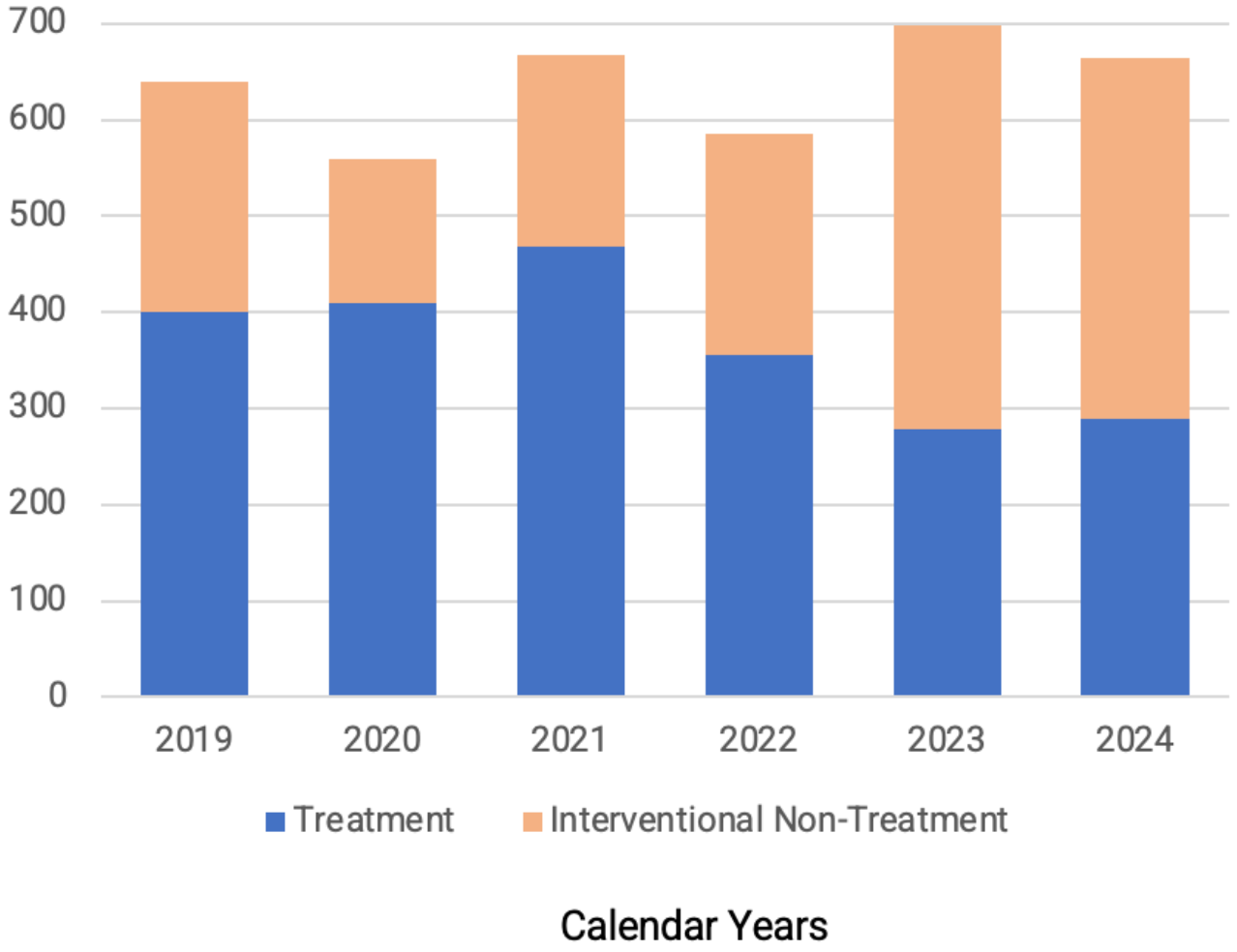
Clinical Research Support Staff (100 FTE) :

Finance & Audit (10)
Regulatory (14)
Informatics (6)
Protocol Development (3)
Quality & Education (2)
Study Navigation & Pre-Study (2)
Mission & Quad City Satellite Locations (12)
Data Coordination (7)
Laboratory Assistants (5)
Consenters (3)
Research Coordinators (36), divided into seven pods.
- Early phase & Leukemia
- Cellular Therapy & Lymphoma
- Myeloma
- GU/Breast/GYN
- GI/Thoracic
- Melanoma/Sarcoma/Head & Neck/Neuro
- Supportive Oncology

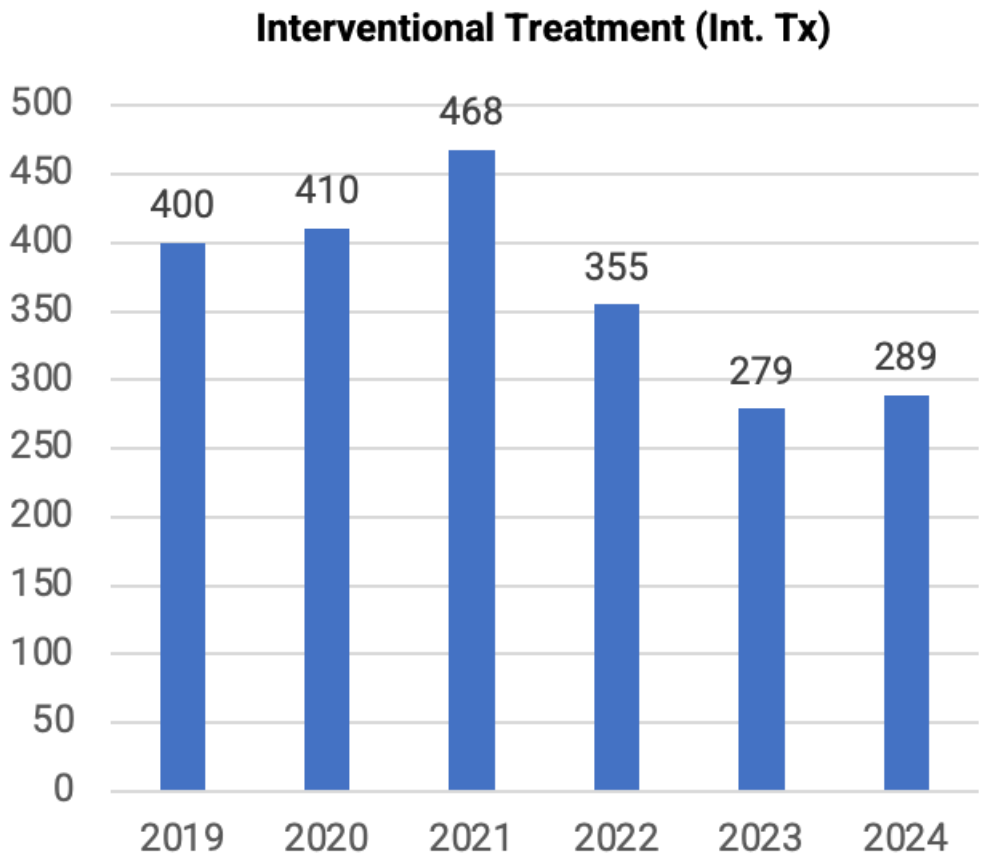
Update From Last Review

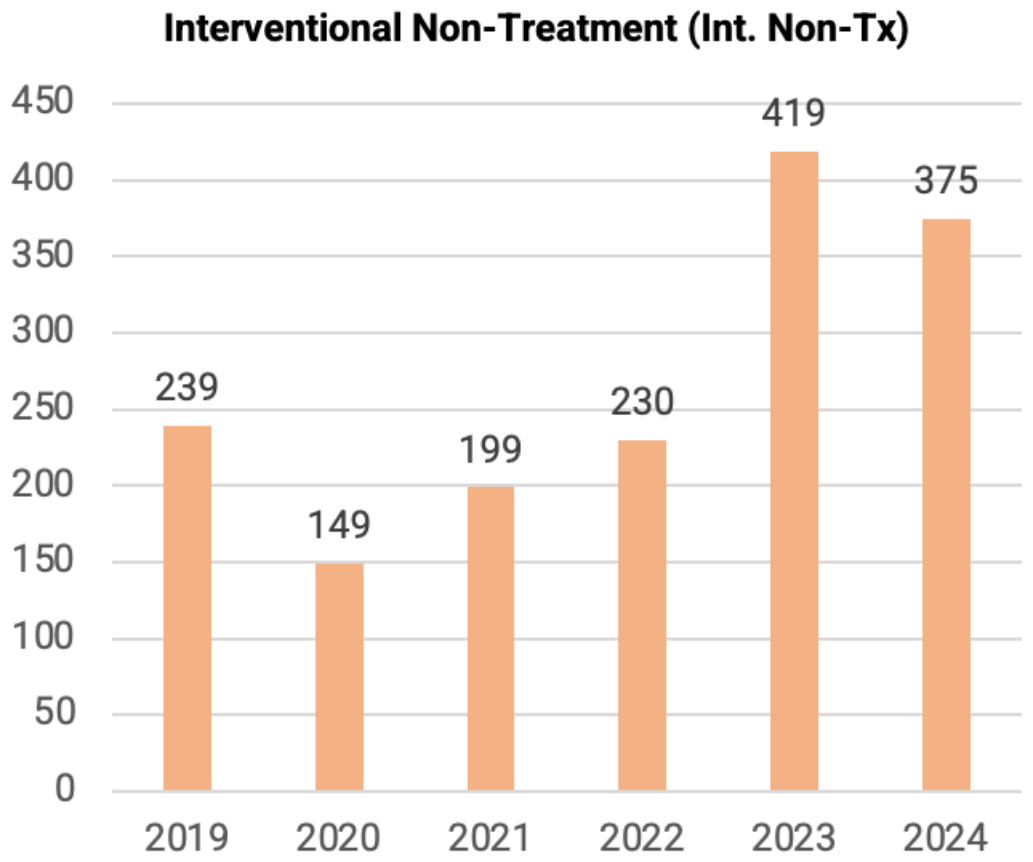
2020 NCI Site Visit	2023 EAB Visit	Steps taken / in progress
Low accruals compare to new analytical cases	Need to recruit clinical research faculty in several disease areas and implement processes to retain faculty.	• Six new faculty hired in GU, GI, Neuro, and Leukemia. Continuing recruitment effort to hire more investigators for GU, GI, and Early Phase Director.
		• Faculty has 30-40% protected time. However, they had to absorb the clinical workload of faculty who left the institution, which impacted their research time.
	Thought should be given to establishing financial models for allowing clinicians to have adequate protected time to engage in clinical research activities.	• Increased engagement with investigators and multidisciplinary oncology group (MOG) leaders
		• Structured training of new faculty members to get them up to speed on clinical research (Dr. Doug Laux)
	Trial activation timelines are fluctuating and long.	• The Human Subject office implemented a system in the summer of 2024 that allows parallel review of clinical trials by multiple stakeholders.

Interventional Accrual



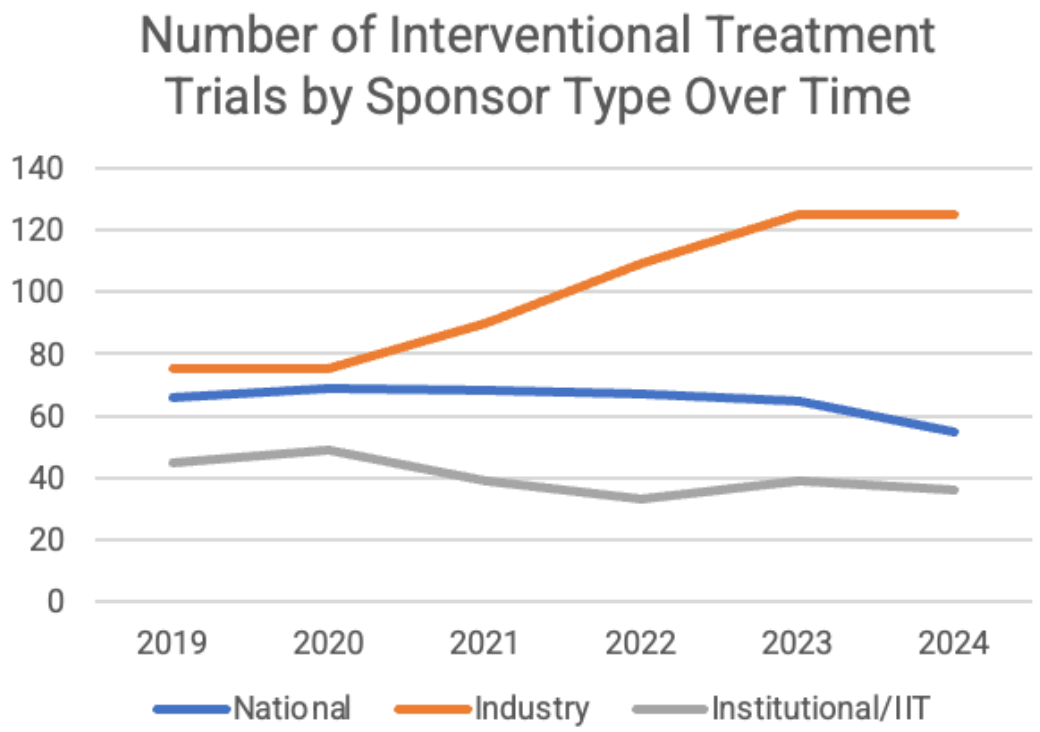
Interventional Accrual

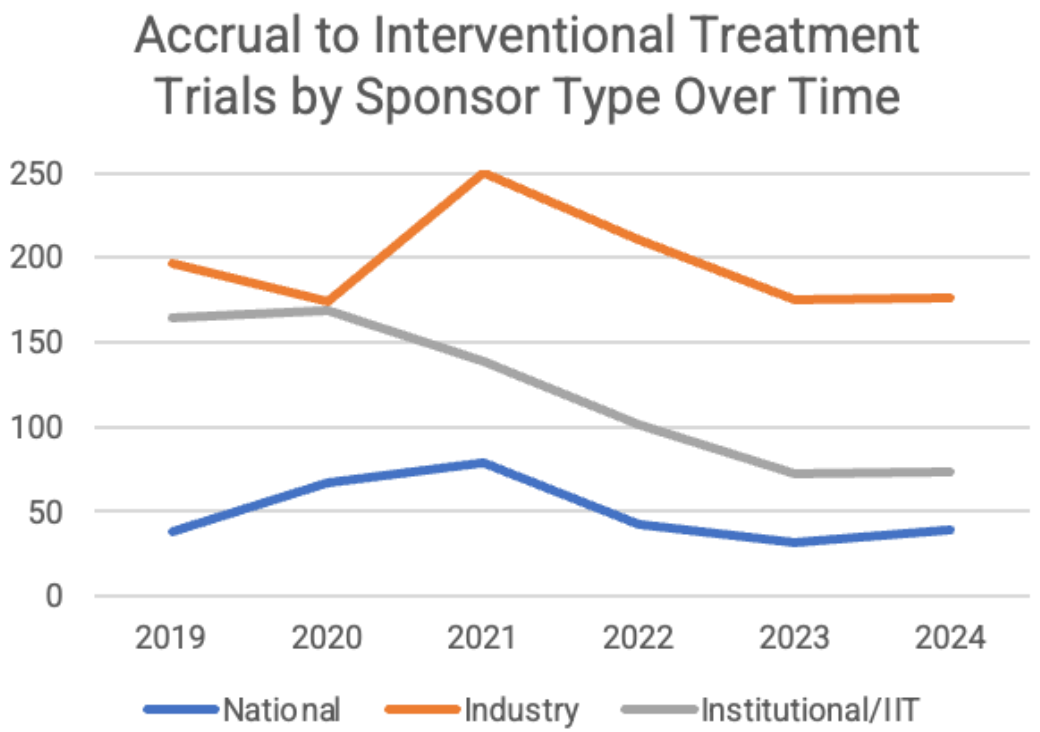




Calendar Years

Treatment Trials & Accrual Trends by Sponsor



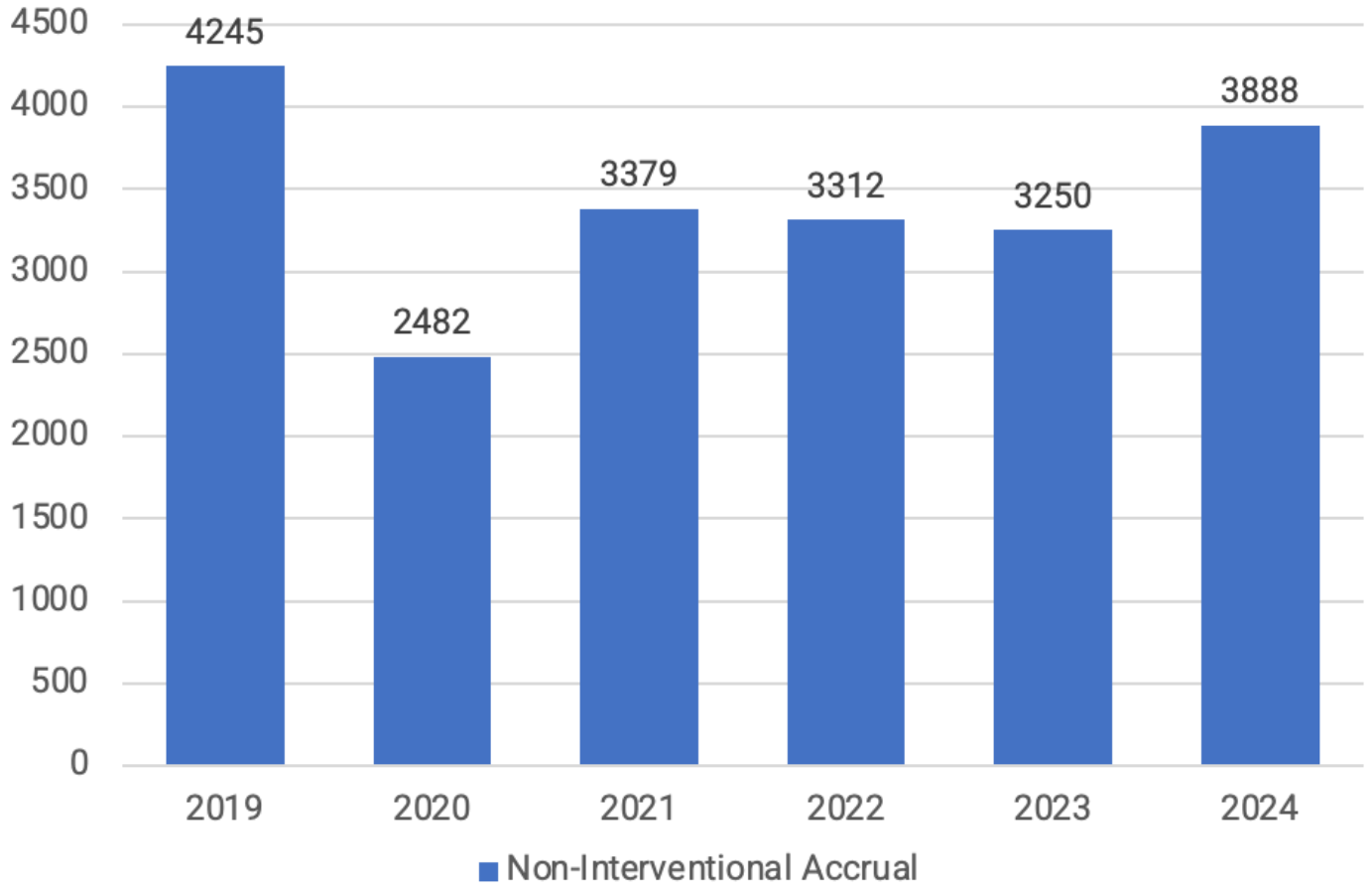


Recruitment Efforts

Faculty*	Rank	Joining Date	Multidisciplinary Oncology Group (MOG)
Gustavo Fernandes Almeida	Asst. Prof	Nov 2024	Neuro-Oncology
Fernando Maciel	Assoc. Prof	Feb 2025	GU
Ioannis A Voutsadakis	Assoc. Prof	April 2025	GI
Mariana Pilon Capella	Asst. Prof	May 2025	GI, Breast
Maria Siddiqui	Asst. Prof	June 2025	Leukemia
Vitor Vasconcellos	Asst. Prof	July 2025	GI, GU

* The offer is out for the Phase I Director. Active recruitment efforts are ongoing to hire additional faculty in GI, GU and a neuroendocrine-focused medical oncologists.

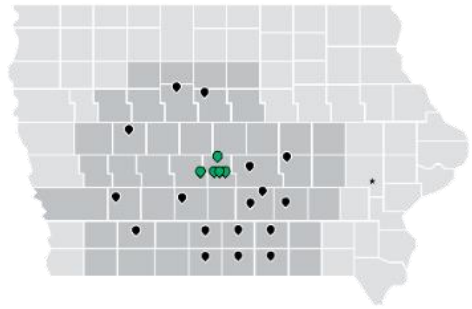
Non-Interventional Accrual

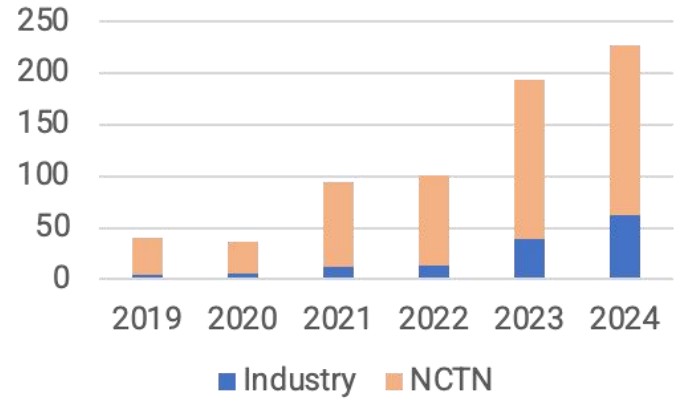


Accrual to observational + ancillary/correlative protocols

Acquisition of 'Mission Cancer & Blood'

- Occurred on Jan 1st, 2025
- Team of nineteen oncologists and > 15 APPs
- EMR and Oncore Integration, expected in June 2025
- Engaging investigators from the Mission to HCCC MOGs Research meetings.
- Working on expanding Mission's trial portfolio through both new trials and older studies open at HCCC.
- NCTN studies open at Mission are through the Iowa Oncology Research Association (IORA), an NCORP
  - IORA NCORP has requested a 10 months extension
  - Planning for having a Minority/Underserved NCORP





Accruals by Calendar Years*

* Includes both therapeutic vs non-therapeutic interventional accruals

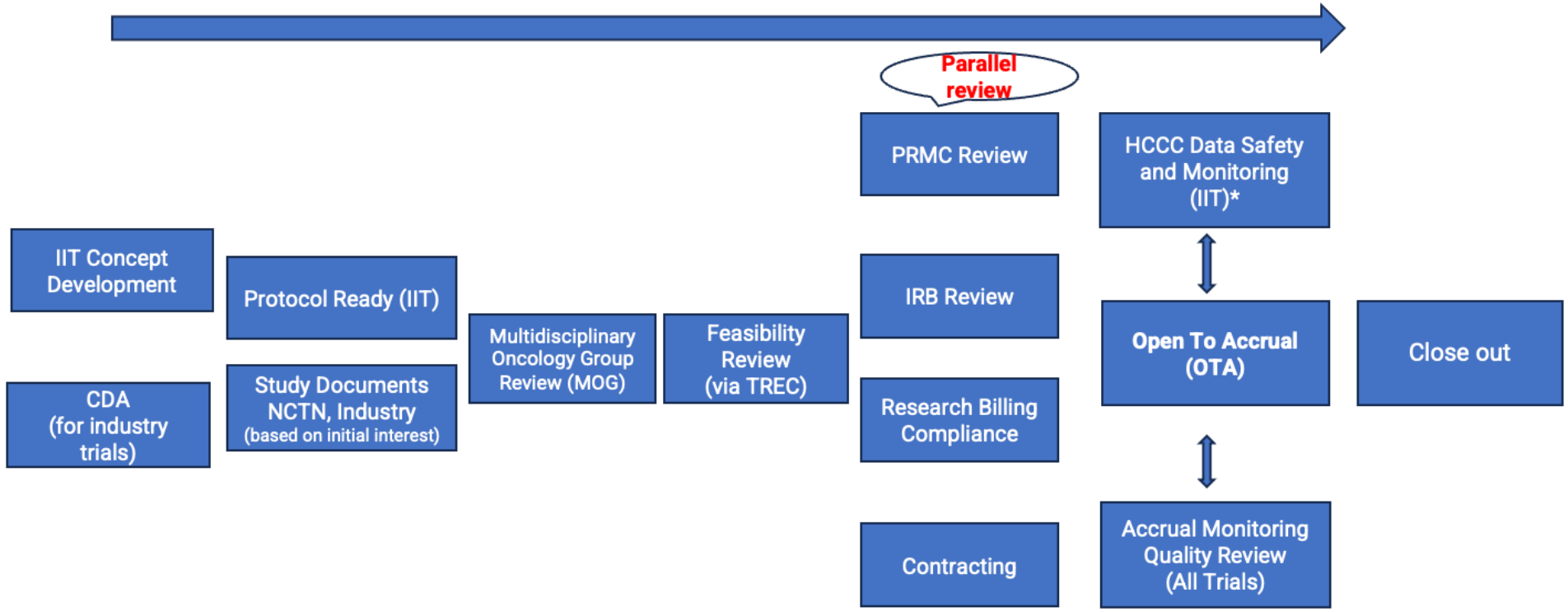
Tara Graff, DO Medical Director for Clinical Research

Shannon Benson, MSN Administrative Director

Communication & Engagement

Weekly	Bi-Weekly	Monthly	Quarterly or Bi-Annual
Dr. Burkard and M. Furqan	CRS Operational Meetings	Clinical Research leadership and MOG leaders' meetings (new meeting – March 2025)	Investigator-retreats
MOGs Investigators Meetings	Trial Resources Evaluation Committee (TREC): Assesses trials' feasibility and required resources	MOG investigators and CRS staff to review portfolio, trials in pipeline and activation process, etc.	Educational meetings
Investigators & Research Coordinators meetings		COE and Clinical Research	

Protocol Development, Review Process & Navigation



* NCTN and industry trials have separate & external data-safety monitoring boards and are reviewed by HCCC DSM as needed.
CDA - confidentiality disclosure agreement; IIT - investigator initiated trials; MOG – multidisciplinary oncology groups; PRMC – protocol review and monitoring committee; IRB – Institutional Review Board (includes external (Advarra and WCG) and internal IRBs (HawkIRB))

Trials Activation Timeline

PRMC Submission to OTA by Sponsor Type (median number of days)				
	IITs	**Industry**	**NCTN**	**All**
2019 (n=98)	149	147	98	129
2020 (n=65)	176	171	82	125
2021 (n=79)	126	156	56	135
2022 (n=88)	340	205	86	199
2023 (n=85)	131	172	59	139
2024 (n=97)	99	137	48	116

PRMC – protocol review and monitoring committee; OTA – open to accrual

New Initiatives (2024-Current)

- Strengthened the support for IITs (including funding support & mentorship)
    - 2024 - 5 LOIs were supported / out of 10
    - 2025 - plan to support 7/ out of 12
    - Established an IIT Development Oversight Committee: to help investigators materializing their LOI to an active trial
- Restructured the research coordinators support: Assigned coordinator lead for each MOG
- Pre-screening (being done manually). Evaluating electronic prescreening tools (Evidently & Triomics)
- Training Mission Cancer and Blood staff on University processes (ongoing)
- Dedicated faculty leader and staff for investigator & staff education (Jan 2025)
- Monthly MOG leaders and clinical research leadership meetings (started in March 2025)

Data Safety and Monitoring (DSM) Update

2020 NCI Site Visit Critique	2023 EAB Visit	Steps taken
Definition of a quorum	Required % for voting members	• Implemented new quorum requirements, a total of nine voting members • 2/3rds voting members

Data Safety and Monitoring Committee (DSMC)

Meets every 6 weeks

Committee Composition:

2 Full Professors
5 Associate Professors

Roles included:
Investigators
Biostatisticians
Pharmacist
Research Coordinators

Quorum:
The committee is comprised of 9 voting members.
2/3rd of voting members

DSMC Leadership:

Chair:
Douglas Laux, MD, MS
Clinical Associate Professor, Internal Medicine-Hematology, Oncology, and Blood and Marrow Transplantation

Co-Chair:
Carryn Anderson, MD
Clinical Professor, Radiation Oncology

Administrative staff:
Cena Jones-Bitterman, MPP, CIP, CCRP
Assistant Director, Compliance and Informatics

Jill Wegmann, RN, BSN, CCRP
Protocol Development and Monitoring Manager

Data Safety and Monitoring

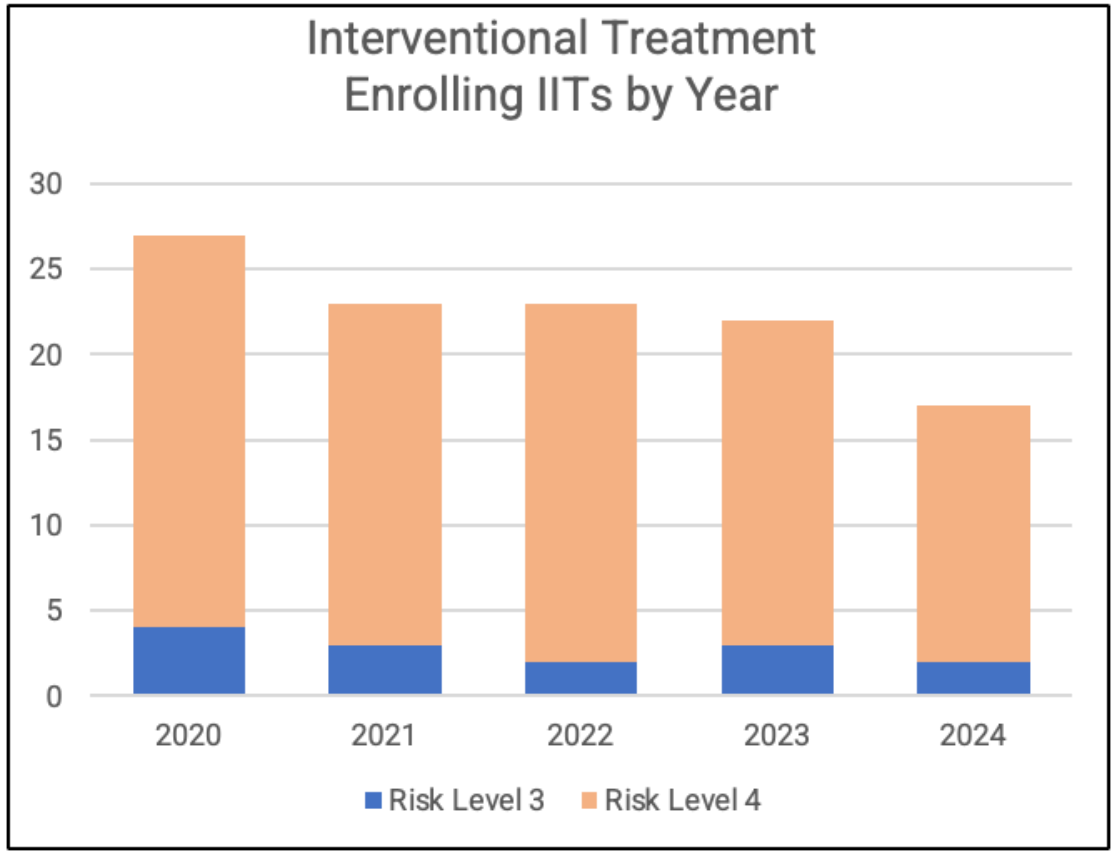
Primary goals: safety, integrity of data, and protocol compliance

- Annual and bi-annual data and safety monitoring for IITs
- Risk level 4 trials that involve INDs are at highest risk and monitored at least twice each year

DSMC provides oversight for trials in the following colleges and departments:

- College of Dentistry, College of Nursing, Psychology, Health & Human Physiology, Urology, Radiology

DSMC Oversight & Monitoring



Protocol Review & Monitoring System (PRMS) Update

2020 NCI Site Visit	2023 EAB Visit	Steps taken / in progress
Low quorum for PRMC	Quorum to be % of total instead of an actual number	• Established PRMC core membership and quorum is 2/3rds of voting members • COE representation at meetings

PRMS – Stage 1 Review Process

Stage 1 review: Completed through the MOG members and leaders

MOG	Leader(s)
Breast	Ingrid Lizarraga, Sneha Phadke
GI	James Howe
GU	James Brown
Gyn Onc	David Bender
Head & Neck	Nitin Pagedar, Doug Laux
Leukemia	Grerk Sutamtewagul
Lymphoma	Umar Farooq, Eric Mou
Melanoma	Mohammed Milhem, Hisakazu Hoshi
Myeloma	Chris Strouse
Neuro Onc	John Buatti
Pediatrics	David Dickens, Jenna Gedminas
Sarcoma	Benjamin Miller, Mohammed Milhem
Thoracic	Kalpaj Parekh, Muhammad Furqan
Early Phase	Recruiting -TBD

Reason for Declining Trials	2022 Reviewed = 211	2023 Reviewed = 374	2024 Reviewed = 266
Lack of interest	35	26	42
Competing studies	34	53	28
Not alligned with catchment area need	11	25	11
HCCC was not selected as site	13	27	24
Protocol concerns	0	9	16
Multiple/other	55	78	71
Total Declined (%)	147 (70%)	218 (58%)	192 (72%)

Multidisciplinary oncology group review is critical in trial selection process. ~60-70% of all trials are declined.

PRMS – Stage 2 Review Process

Stage 2 review: Completed through the Protocol Review and Monitoring Committee (PRMC)

Meets twice monthly

Committee Composition:

5 Full Professors
6 Assoc. Professors
2 Biostatisticians
2 Pharmacists
1 Patient Advocate

Review requirements:

All interventional protocols require 2 scientific, 1 pharmacy, and 1 biostatistical reviewer

Quorum:
2/3rd of voting members

Accrual Monitoring Policy (revised SOP* 2024):

Trials queried at 3- and 6-months following OTA
Expect 60% of accrual goal achieved 1-year following OTA

*SOP – standard operating procedure

PRMC Leadership:

Chair:
Michael Goodheart, MD
Professor of Gynecologic Oncology
Director, Division of Gynecologic Oncology
Fellowship Director, Division of Gynecologic Oncology,
Department of Obstetrics & Gynecology

Co-Chair:
C. Michael Knudson, MD, Phd
Professor of Pathology
Medical Director of the DeGowin Blood Bank

Administrative staff:
Cena Jones-Bitterman, MPP, CIP, CCRP
Assist. Dir. Compliance & Informatics

Angela Childs, BA, CCRP
Protocol Mgmt. Specialist

Dagem Adera, BA
PRMC Coordinator

PRMC: Accrual Monitoring

Accrual Monitoring Activity (2020-2024)					
	2020	2021	2022	2023	2024
Trials queried	17	27	36	31	39
Trials closed	1	7	8	15	7
Rare cancer	1	1	3	2	0
Keep Open – Other reasons	15	13	25	22	26
3-month warning letter	N/A	5	7	19	25

*Trials may be queried multiple times

REASONS SLOW ACCRUING TRIALS KEPT OPEN

- Narrow eligibility population, ever decreasing denominator
- Dose-escalation studies with stop-go-stop
- Ongoing enrollment efforts being made (e.g. patients screened, enhanced recruitment plan developed)
- Amendment in progress to address eligibility

Inclusion in Clinical Research

- Inclusion of Women
- Inclusion of Rural Population
- Inclusion of Racial and Ethnic Minorities and Across the lifespan (see Additional Slides)

Inclusion of Women in Clinical Research

	2019	2020	2021	2022	2023*	2024*
HCCC % New Women patients (HCCC registry data/new patients)	50%	48%	50%	49%	49%*	49%*
Interventional Treatment [1]**	41%	45%	47%	45%	41%	38%
Interventional Non-Treatment [2]	53%	56%	76%	59%	65%	74%
Non-Interventional [3]	50%	49%	48%	52%	59%	63%

*Estimate based on 2022 analytical cases

[1]Calculated as total women enrolled in treatment trials/total number of participants enrolled in treatment trials
[2]Calculated as total women enrolled in non-treatment interventional trials/total number of participants enrolled in non-treatment interventional trials
[3]Calculated as total women enrolled in non-interventional trials/total number of participants enrolled in non-interventional trials

Inclusion of Women in Clinical Research

(Excluding sex-specific cancers)*

	2019	2020	2021	2022	2023	2024
HCCC % New Women patients (HCCC registry data/new patients)	43%	41%	43%	43%	43%**	43%**
Interventional Treatment [1]**	38%	42%	44%	41%	37%	34%
Interventional Non-Treatment [2]	50%	44%	49%	52%	60%	66%
Non-Interventional [3]	49%	48%	48%	48%	50%	54%

*Breast, Gyn Onc, Prostate, and other sex-specific cancers removed

**Estimate based on 2022 analytical cases

[1]Calculated as total women enrolled in treatment trials/total number of participants enrolled in treatment trials
[2]Calculated as total women enrolled in non-treatment interventional trials/total number of participants enrolled in non-treatment interventional trials
[3]Calculated as total women enrolled in non-interventional trials/total number of participants enrolled in non-interventional trials

Inclusion of Women: Analysis and Actions

Possible Reasons	STEPS TAKEN/IN PROGRESS
Low accrual appears to widen the gap (B. McDowell – CEPS). There is a difference in the 'sex' mix in the analytical cases vs. patients in the clinic for which a trial option is available of about ≈ 2-3% (M. Furqan)	Increased awareness across investigators and research staff regarding this issue. A report is provided every quarter. Women are prioritized for prescreening. Recruiting a medical oncologist with a Gyn-oncology focus to help women accrual Engaging COE and CAB members for partnership & help in spreading the word to the communities and better caregiver support for women Collaborating with CEPS members in analyzing registry and enrollment trends Educational training on 'Implicit Bias' for all investigators and research staff

Inclusion of Rural Patients in Clinical Research

	2019	2020	2021	2022		2024
Rural patient proportion in HCCC analytical cases[1]	42.4%	42.9%	41.9%	43.3%	Not available	Not available
All Interventional[2]	33.6%	33.5%	28.7%	34.7%	35.9%	38.4%
Interventional Treatment[3]	38.0%	38.9%	35.5%	38%	39.8%	42.7%
Interventional Non-Treatment[4]	26.4%	18.9%	16.0%	29.4%	33.1%	34.3%

[1] Calculated as Rural patients in HCCC Oncology Registry / Total Patients in HCCC Oncology Registry
[2] Calculated as rural patients in interventional trials / Total patients in all interventional trials (113 participants were excluded due to missing rurality data)
[3]Calculated as Rural patients in interventional treatment trials / Total patients in interventional treatment trials category
[4]Calculated as Rural patients in interventional non-treatment trials / Total patients in interventional non-treatment trials category

Patients residing in counties with Rural Urban Continuum Code of 4-9 were considered rural

Goals

- Getting new investigators up to speed and recruiting faculty for the Early Phase Program and GU

- Increase interventional accrual (HCCC)
  - 2025 - for therapeutic ≥ 325 , Non-therapeutic ≥ 431
  - 2026 - for therapeutic ≥ 370 , Non-therapeutic ≥ 490

- Expand HCCC trial portfolio to Mission Cancer and Blood to improve access and increase accrual
  - Goals: Assess all new studies for activation at Mission and improve their capabilities for conducting complex trials.
  - Open IITs over there and be able to monitor those

- Pre-screening:
  - Priority MOGs: Gyn-Onc, GU, GI, Breast patients by July 2025
  - All MOGs: Dec 2025
  - Implement an electronic platform (Evidently or Triomics)

- Continue to provide funding and infrastructural support for IITs

- Continue to improve the activation timeline

- Improve staff retention

- ETCTN membership (Q1 2026)

Clinical Research Discussion

Additional Slides (# 29-38)

- CPDM (slides # 30-33)
  - Percent accrual of specific patients in interventional trials
  - Increase in trial complexity in therapeutic space
  - Trends in interventional non-therapeutic trials and accruals by sponsor
  - Staff recruitment & retention efforts

- Inclusion in Clinical Research (# 34-38)
  - Inclusion of minorities in clinical research
  - Inclusion of Children, AYA and 65+ in Clinical Research (# 36-38)
  - Percentage of HCCC women, children, AYA, +65 participating in trials

Percent Accrual of Patients With a Specific Disease*

Int. Tx. Accrual / Registry Cases*	2019 (%)	2020 (%)	2021 (%)	2022 (%)	2023** (%)	2024** (%)
Breast	1.0	2.2	4.2	1.8	0.9	3.0
GI Onc	3.9	10.8	8.2	3.9	3.9	4.2
GU Onc	9.0	7.3	4.5	3.4	3.6	1.9
Gyn Onc	3.6	4.1	2.9	3.2	2.0	1.4
Head and Neck	4.1	5.2	3.4	2.5	1.7	6.9
Leukemia	19.9	50.0	54.2	17.7	7.4	6.0
Lymphoma	9.4	10.5	10.9	10.9	11.2	11.7
Melanoma	13.0	10.5	10.2	8.3	7.1	4.3
Myeloma	4.1	5.6	21.6	11.8	17.2	24.7
Neuro Onc	9.0	6.2	6.6	5.1	2.4	2.9
Sarcoma	26.4	18.7	25.2	25.1	14.4	5.1
Thoracic Onc	11.0	19.2	12	10.7	9.3	12.0
Average	8.0	9.8	9	8.7	6.8	7.0

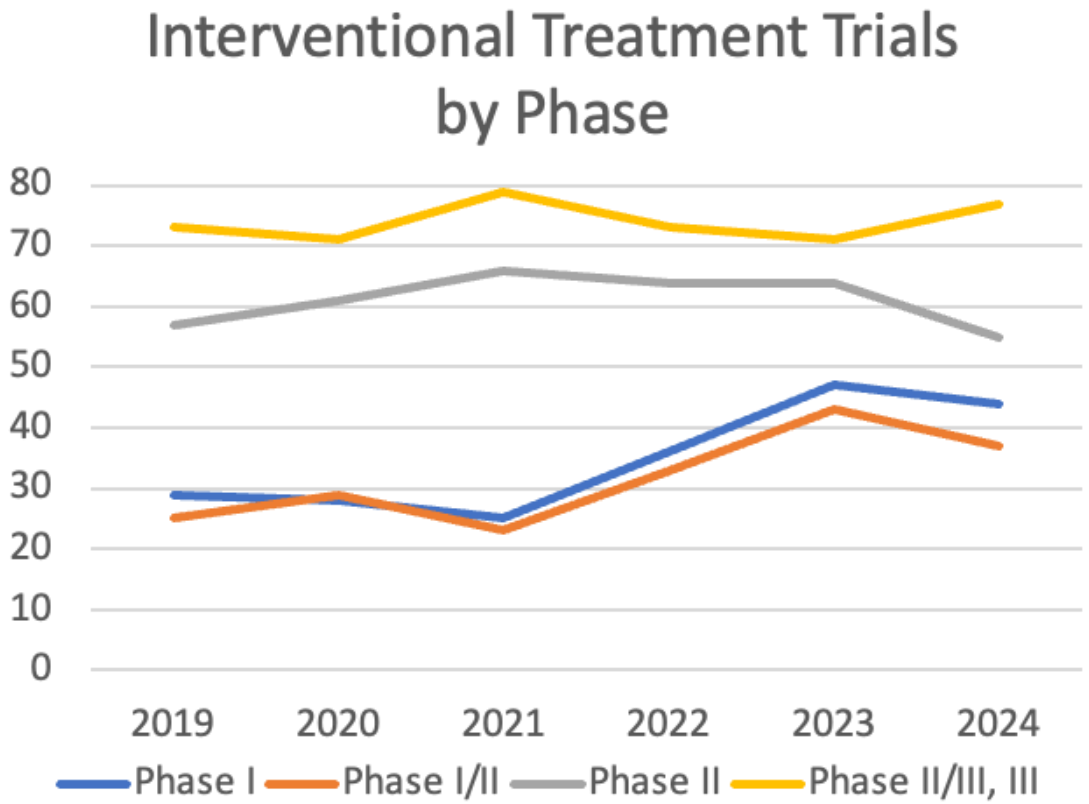
Int. Non-Tx./ Registry Cases*	2019 (%)	2020 (%)	2021 (%)	2022 (%)	2023** (%)	2024** (%)
Breast	10.0	6.1	16.9	2.1	7.8	10.6
GI Onc	3.8	0.0	0.0	0.1	5.3	0.7
GU Onc	4.6	1.4	0.9	2.1	3.3	2.2
Gyn Onc	1.7	4.2	8.6	7.5	9.5	9.3
Head and Neck	2.4	3.8	1.1	9.5	29.8	28.2
Leukemia	3.0	3.5	10.5	22.8	7.4	4.7
Lymphoma	6.7	2.6	2.0	3.7	2.9	1.4
Melanoma	2.0	0.0	0.0	0.6	0.6	0.3
Myeloma	4.1	0.0	0.0	0.0	2.2	7.5
Neuro Onc	.5	0.3	1.3	1.8	0.9	0.9
Sarcoma	5.0	7.7	8.3	6.7	7.7	1.0
Thoracic Onc	3.1	6.6	0.6	0.0	0.8	0.8
Average	4.8	3.5	3.7	4.7	6.5	5.6

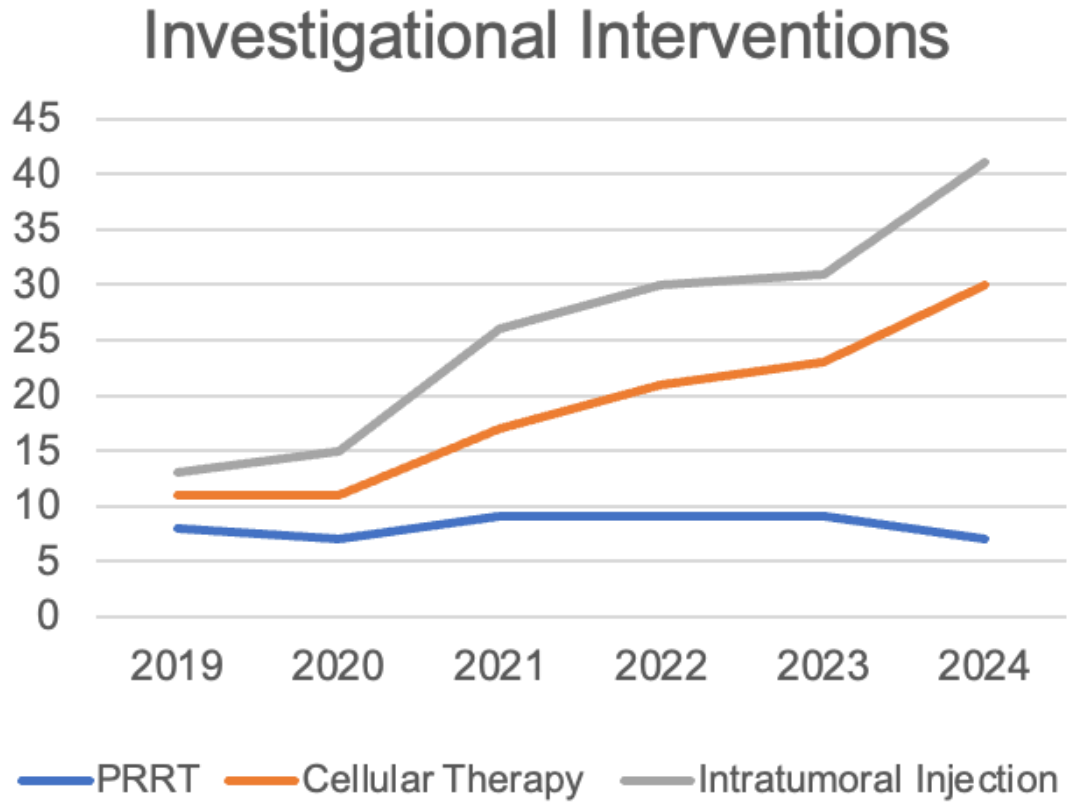
Goals: > 15% for each category, interventional therapeutics and non-therapeutics.
*Accrual of patients with a specific disease/ Number of new analytical cases with a specific disease;
** HCCC analytical cases from 2022 were used for calculation

Analytical Cases (00-22, 32)

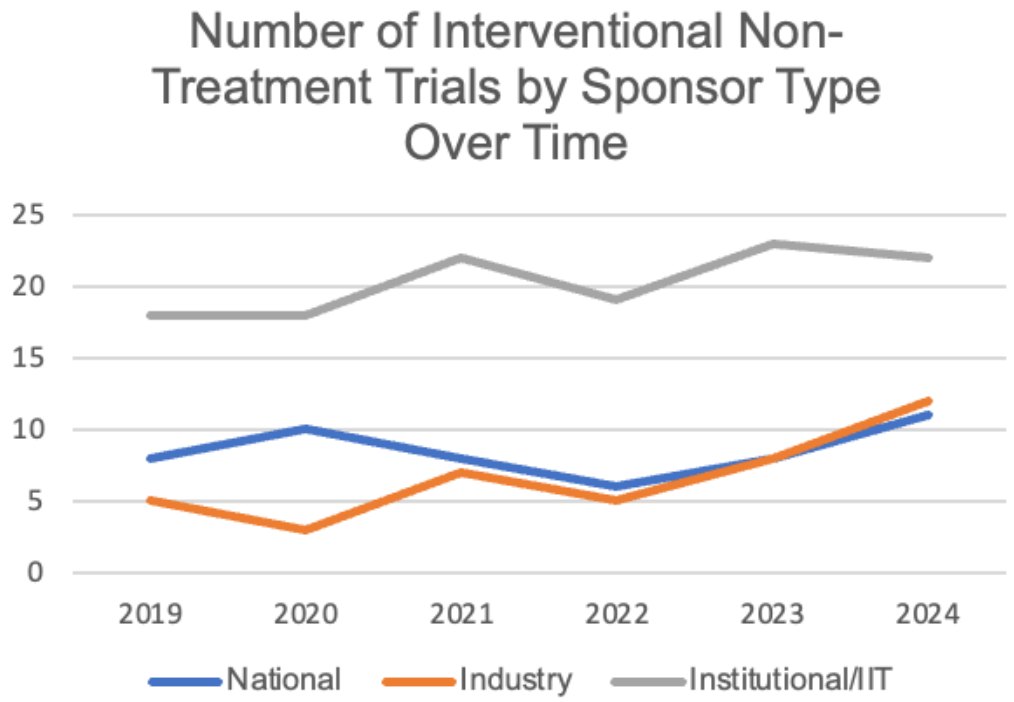
2019: 5226 2021: 5205
2020: 5047 2022: 5681

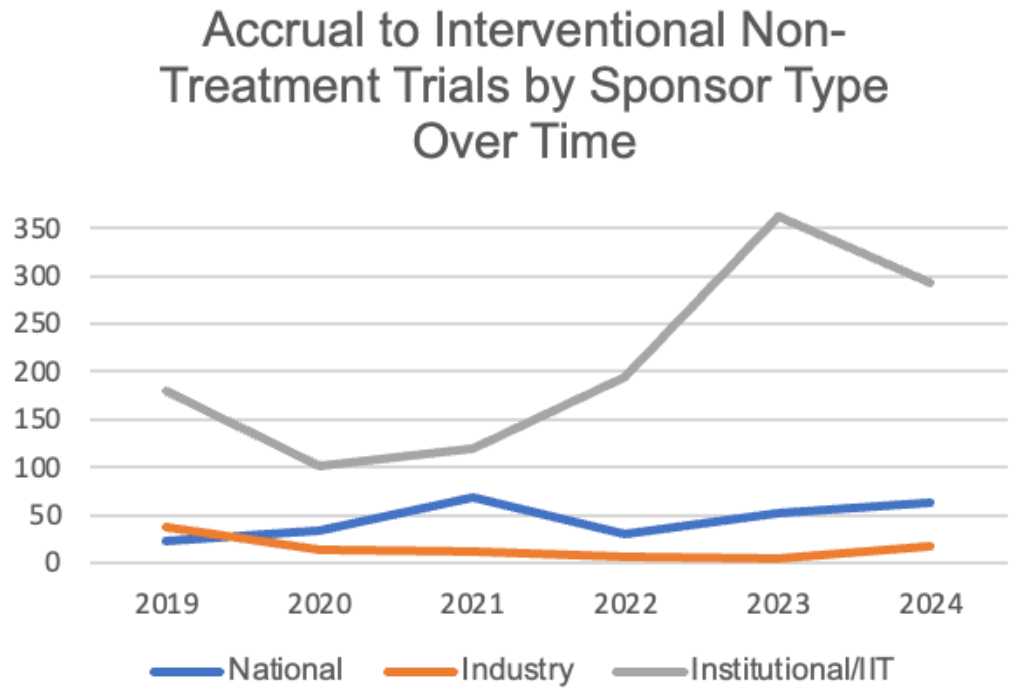
Trials' Complexity – By Phase And Intervention Type





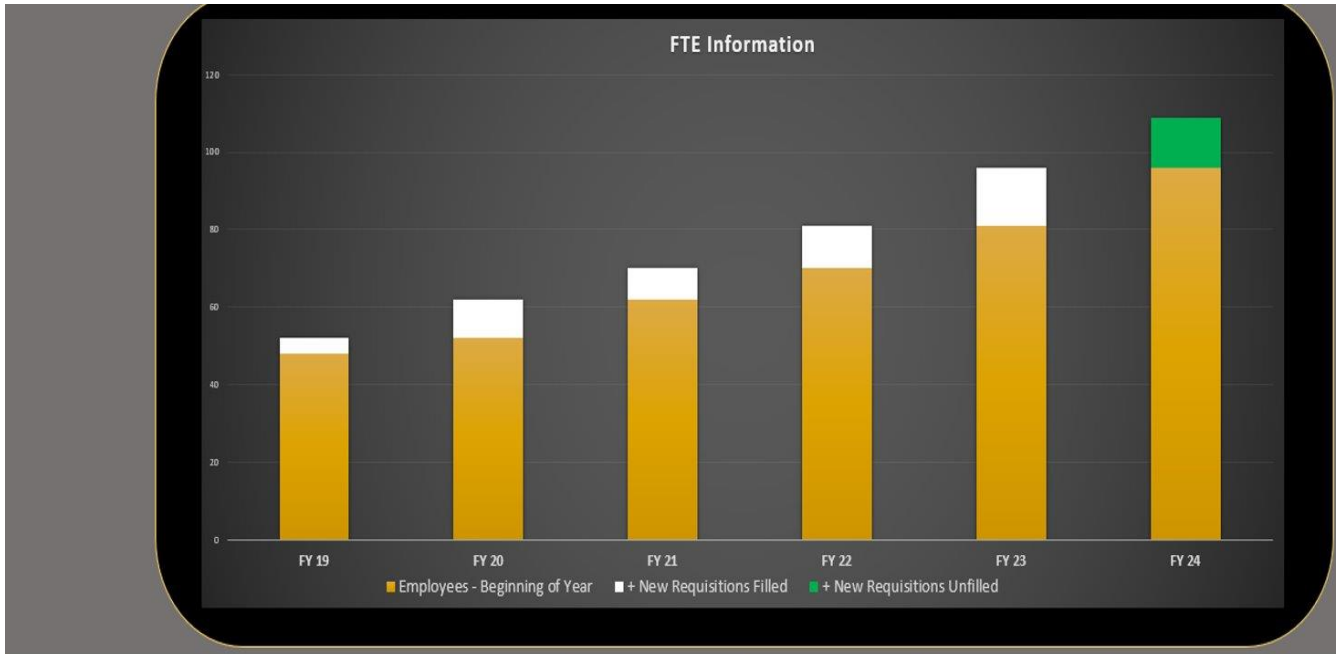
Interventional Non-Treatment Trials and Accrual





- IITs in this space typically sponsored in the past by extramural funding. The IITSI award will also support these trials, and we expect an increase in them. New leadership and MOG for supportive-care trials.

Clinical Trials Office Recruitment and Retention



	FY 19	FY 20	FY 21	FY 22	FY 23	FY 24
Employees - Beginning of Year	48	52	62	70	81	96
+ New Requisitions Filled	4	10	8	11	15	0
+ New Requisitions Unfilled	0	0	0	0	0	13
Employees - End of Year	52	62	70	81	96	109
Turnover	Unknown	Unknown	Unknown	24	17	3
				30%	18%	3%

Key Retention Initiatives in 2023-2024

- External coach to improve work culture
- Successful migration to a hybrid work model for all non-patient-facing teams
- Finalizing career ladder
- Flex Awards 10% of base salary for all high-performing staff
- ***Turnover has dropped from 30% to about 3% in 2024.***

Inclusion of Minorities in Clinical Research

	Women	American Indian/ Alaska Native	Asian	Native Hawaiian or Pacific Islander	Black or African American	White	More than One Race	Unknown/ Not reported	Hispanic or Latino
Iowa Census (2020)	49.8%	0.6%	2.8%	0.2%	4.4%	89.8%	2.2%	NA	6.9%
Cancer Incidence (Iowa SEER data)	50.4%	0.2%	0.6%	0.1%	2.0%	97.0%	0.1%	NA	1.3%
HCCC new Analytical Cases(2022)	49%	0.25%	1%	0.23%	3.4%	94%	0.4%	0.6%	3.1%
Interventional, Treatment	38%	0.35%	0.35%	0%	1.39%	92.8%	0%	4.6%	1.7%
Interventional, Non-Treatment	74%	0.3%	1%	0%	3%	92.4%	0%	3.3%	3.0%
Non-Interventional	63%	0.25%	0.5%	0.06%	2.1%	92.8%	0.03%	4.2%	2.1%

Clinical trial enrollment data for CY2024

Children in Clinical Research

	2019	2020	2021	2022	2023	2024
HCCC % New Peds patients (HCCC registry data/new patients)	2%	2%	2%	1.5%	1.5%*	1.5%*
Interventional Treatment Accruals[1]	4%	4%	7%	6%	5%	5%
Interventional Non-Treatment Accruals[2]	0.4%	1%	11%	19%	4%	1%
Non-Interventional Accruals[3]	4%	6%	3%	3%	4%	3%

*Estimate based on 2022 analytic cases

[1]Calculated as total peds enrolled in treatment trials/total number of participants enrolled in treatment trials
[2]Calculated as total peds enrolled in non-treatment interventional trials/total number of participants enrolled in non-treatment interventional trials
[3]Calculated as total ped enrolled in non-interventional trials/total number of participants enrolled in non-interventional trials

AYA(13-39 Yr. Old) in Clinical Research

	2019	2020	2021	2022	2023	2024
HCCC % New AYA patients (HCCC registry data/new patients)	7%	8%	8%	7.3%	7.3%*	7.3%
Treatment Accruals[1]	13%	13%	16%	10%	9%	6%
Non-Treatment Accruals[2]	21%	28%	18%	36%	16%	7%
Non-Interventional Accruals[3]	11%	16%	12%	9%	8%	9%

*Estimate based on 2022 analytic cases

[1]Calculated as total AYA enrolled in treatment trials/total number of participants enrolled in treatment trials
[2]Calculated as total AYA enrolled in non-treatment interventional trials/total number of participants enrolled in non-treatment interventional trials
[3]Calculated as total AYA enrolled in non-interventional trials/total number of participants enrolled in non-interventional trials

Older Adults (65 Yr. +) in Clinical Research

	2019	2020	2021	2022	2023	2024
HCCC % New 65 YR+ patients (HCCC registry data/new patients)	49%	49%	50%	53%	53%*	53%*
Interventional Treatment Accruals[1]	46%	42%	41%	46%	50%	47%
Interventional Non-Treatment Accruals[2]	25%	25%	37%	37%	42%	45%
Non-Interventional Accruals[3]	46%	41%	46%	47%	47%	48%

*Estimate based on 2022 analytic cases

[1]Calculated as total 65+ enrolled in treatment trials/total number of participants enrolled in treatment trials
[2]Calculated as total 65+ enrolled in non-treatment interventional trials/total number of participants enrolled in non-treatment interventional trials
[3]Calculated as total 65+ enrolled in non-interventional trials/total number of participants enrolled in non-interventional trials

Percent Accrual of Specific Patient-Cohorts in Trials*

	2019	2020	2021	2022	2023	2024
All Patients	12%	11%	13%	10%	12%*	12%*
Women	11%	11%	14%	10%	14%*	13%*
Pediatric (Under 18 Yrs Old)	16%	18%	54%	72%	31%**	20%**
AYA (13-39 Yrs Old)	27%	25%	29%	28%	21%**	9%**
65+ Years Old	9%	9%	10%	8%	10%**	9%**
Rural Patients	10%	9%	10%	8%	10%**	9%**

*Number of accrual of a specific patient cohort to interventional trials/number of HCCC analytical cases in each cohort
**Estimate based on 2022 analytical cases for each cohort