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CANCER RESEARCH NETWORK

Infinite possibilities.

Investigator-Initiated Oncology Trials

TRENDS, CHALLENGES, AND OPPORTUNITIES

Spring 2025

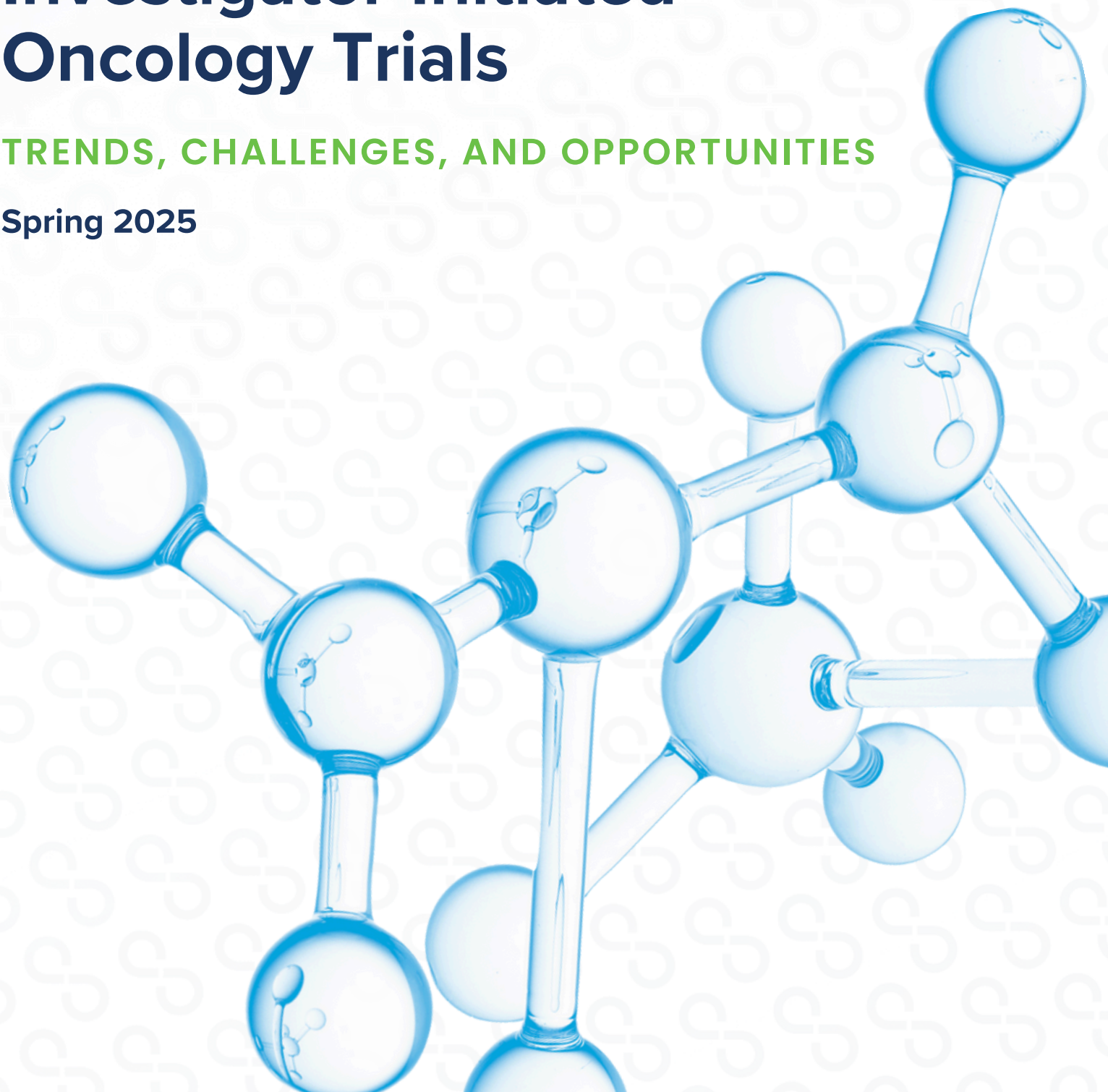


Table of Contents

Abstract

Hoosier Cancer Research Network (HCRN) is a nonprofit contract research organization focused on early-phase, multi-center, investigator-initiated clinical trials (IITs). With a network of more than 100 member institutions and community sites across the United States, HCRN is an example of effective collaboration that has spanned more than four decades of clinical research advances. The research landscape today is vastly different from HCRN's early years, offering both unprecedented opportunities and significant challenges to those who lead and participate in IITs.

In this paper, we report our findings from a survey conducted in late 2024 with HCRN member investigators.

Our goal was to better understand the challenges and successes our members have experienced in leading and implementing multi-site IITs.

The results underscore that IITs serve an important and unique role in the development of novel therapeutic approaches across cancer types. However, there are multiple challenges that hinder the pace of progress, including funding limitations and operational issues that have persisted since the COVID-19 pandemic.

Introduction

Oncology clinical trials in the United States began in earnest in the mid-1950s, when the National Cancer Institute launched its first randomized trial to treat patients with acute leukemia.[1] By the 1960s, many trials were led by cooperative groups with funding and oversight by the federal government or pharmaceutical companies.[2] An alternative to federal or industry-sponsored research, investigator-initiated trials (IITs) emerged as a mechanism by which investigators and their institutions could lead significant independent clinical research.

The Role of CROs

As cancer research continued to develop throughout the late 20th century, the complexity and costs of conducting clinical trials increased significantly. Research sponsors began looking for outsourcing options for data management and biostatistical analysis during periods of high activity.[3] The new entities for outsourcing became known as contract research organizations (CROs). Throughout the 1990s, the scope of services provided by CROs grew to include all aspects of study management, from engagement with investigators to collecting samples for correlative analysis.[4]

What are Investigator-Initiated Trials?

Unlike clinical trials conducted by pharmaceutical, biotech, or commercial contract research organizations, investigator-initiated trials are clinical studies that are initiated and managed by researchers who are typically employed by academic research institutions. These trials are often driven by questions that are left unanswered after industry studies are completed.[5] IITs generate data on the efficacy and safety of a drug, device, or other intervention and attempt to answer questions that clinicians face in their day-to-day practice.[6]

Why are IITs Important?

As a means to conduct independent research, IITs provide an opportunity to evaluate novel therapeutic approaches within a representative sample population seen in clinical practice. Randomized controlled trials, by contrast, are often performed within relatively homogenous populations.[7] While many IITs are conducted at single institutions, there are opportunities for investigators to participate in multi-center collaborative IITs.

Investigator Demographics

We invited investigators across the HCRN network to participate in our survey.

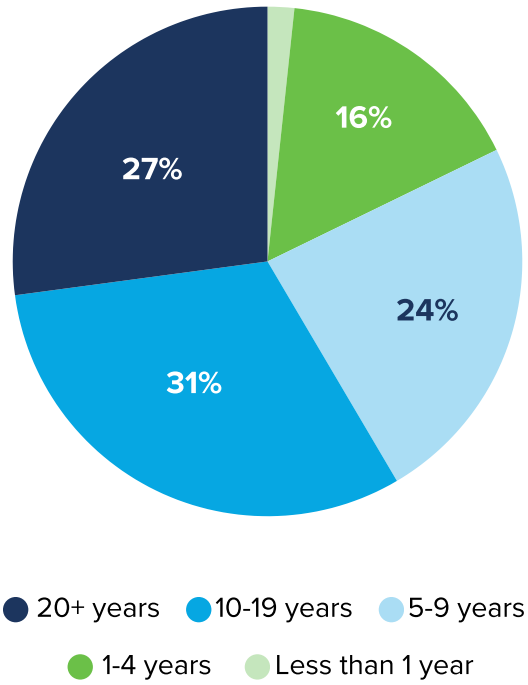
134

investigators responded to our survey

Some notable observations:

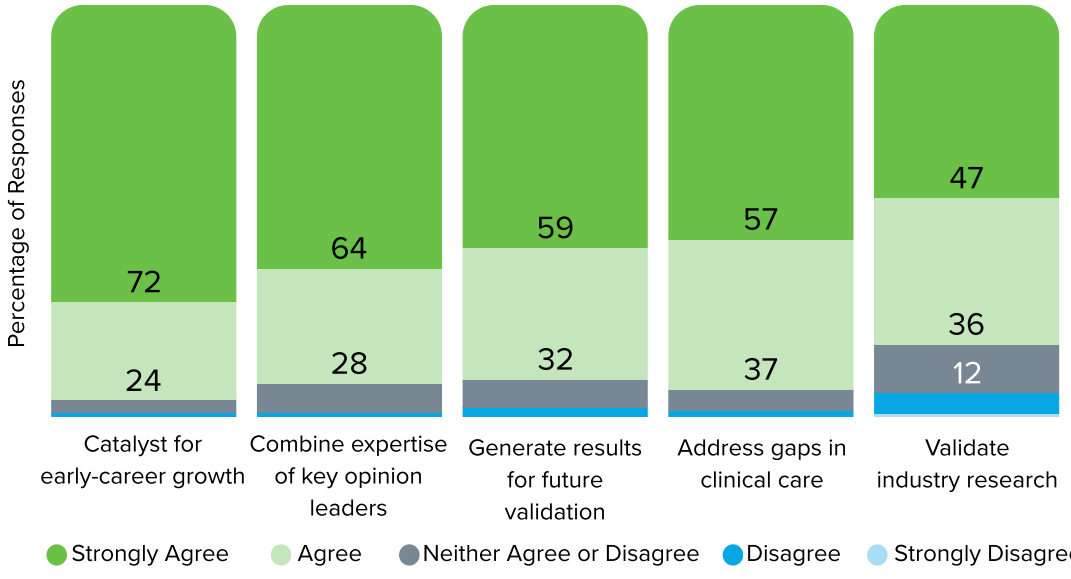
- **120** (90%) have participated in at least 1 IIT.
- **110** (82%) have led at least 1 IIT.
- The majority of these IITs were single-arm, phase I/II, therapeutic interventional studies.
- **78** (58%) report they participated in research that led to local changes in care, changes in national treatment guidelines, or new drug registrations.

The majority of the HCRN network consists of investigators who have been in clinical research for at least 5 years post-residency.

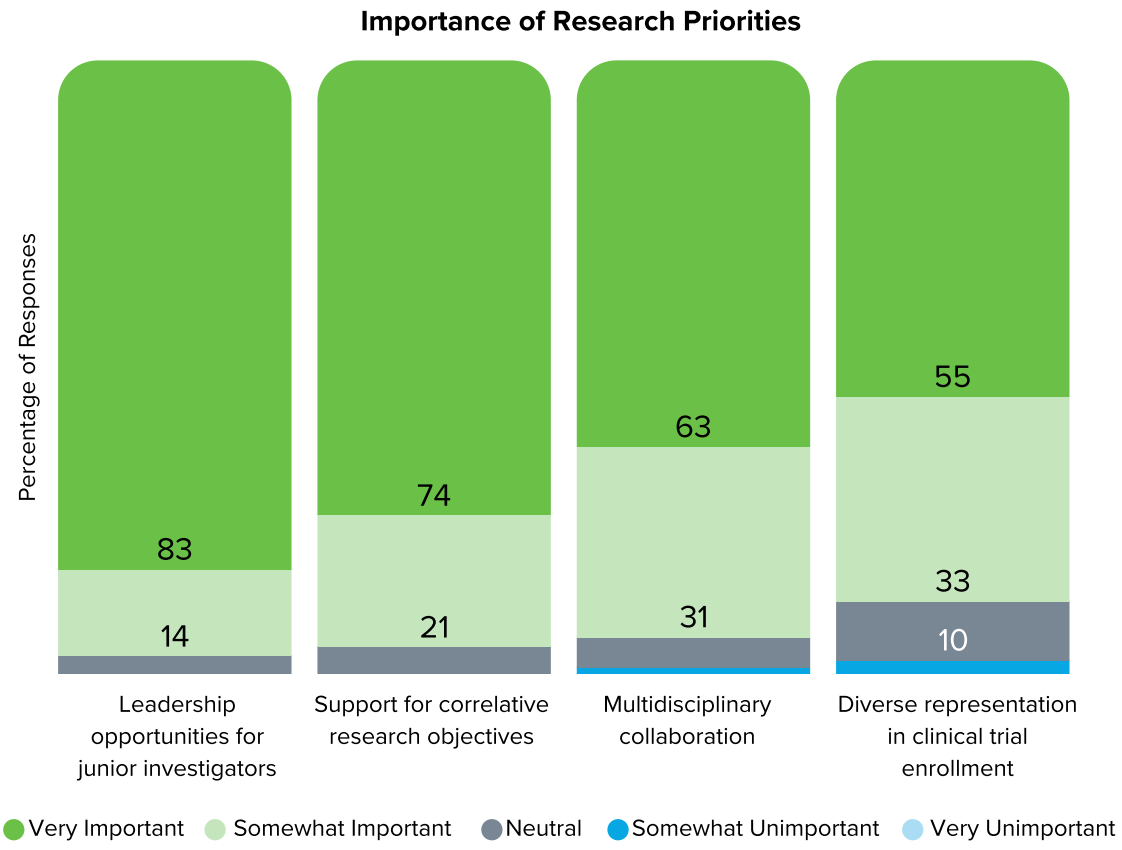


HCRN investigators report that multi-center collaboration can help investigators craft more impactful studies, leverage the strengths of different institutions, and access a broader patient population.

Value of Multi-Center IITs



In addition, IITs create opportunities for junior investigators to contribute significantly to clinical research early in their careers. Through multi-center IITs, these researchers are able to develop their knowledge and expertise by engaging with mentors across institutions. Finally, multi-center IITs allow researchers to study rare populations that cannot be effectively studied at a single institution.



Challenges Impacting IITs

While IITs have contributed significantly to scientific discovery, there are numerous challenges that can hinder the development, activation, and successful completion of these studies. Through our survey, HCRN investigators quantified the degree to which operational, institutional, external, and funding challenges have impacted their studies.

OPERATIONAL CHALLENGES

According to the Tufts Center for the Study of Drug Development, oncology clinical trials are becoming more complex and numerous with an increased focus on patient subpopulations.

Between 2000 and 2020, the number of investigational treatments targeting cancer increased from 412 to 1,489.[8]

More than half of our survey respondents indicated that accrual challenges due to the rarity of the disease have had a moderate to significant impact on their studies. Nearly **half** say the same about stringent eligibility criteria. Insufficient drug availability has hindered some investigators more than others, with about **one-in-five** reporting significant impact and about **25%** reporting moderate impact. In addition, many investigators reported a significant challenge in identifying sufficient participating site interest in their IITs.

"Even after industry-led registration studies are completed, there are often questions about the impact on specific populations of patients. We need to refine which patients will benefit most from a treatment by understanding the biology of treatment and biomarkers to guide treatment selection. While IITs can fill these knowledge gaps, funding remains a barrier, as it can take longer to accrue smaller populations of patients."

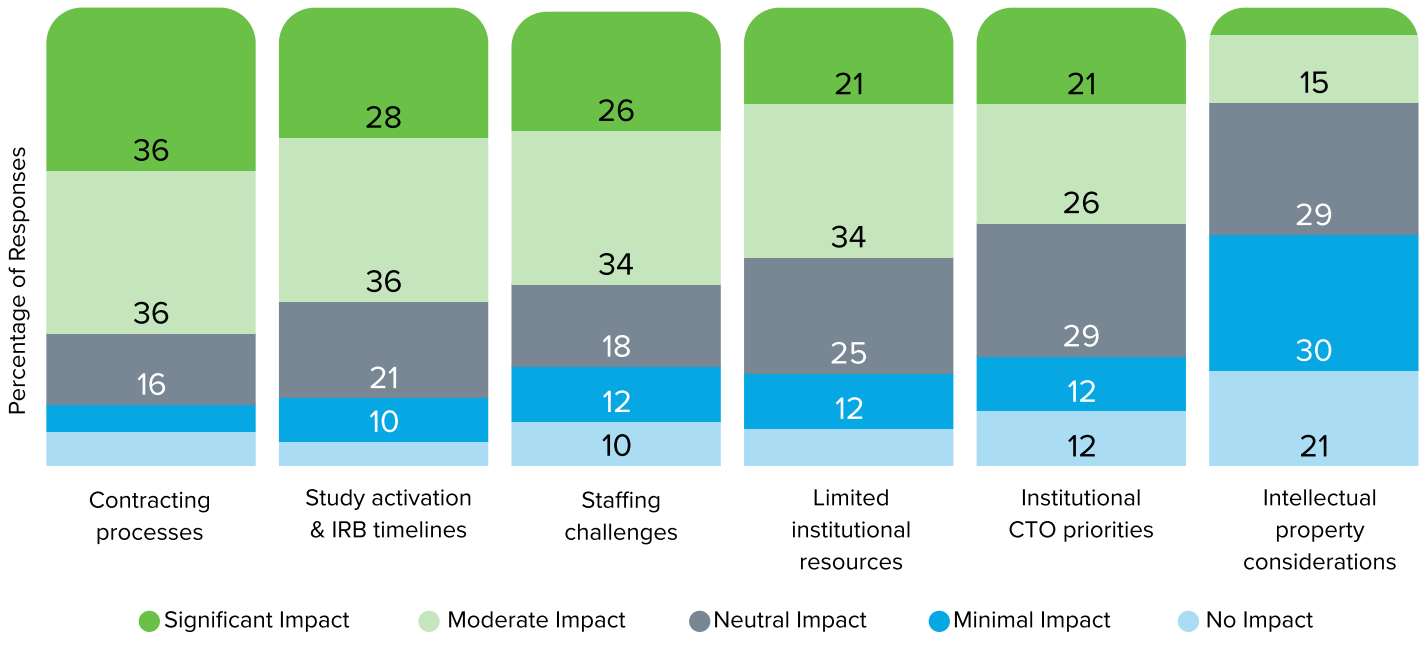
Dwight Owen, MD, MS, The Ohio State University

INSTITUTIONAL CHALLENGES

The majority of HCRN investigators have experienced moderate to significant challenges at their own institutions involving contracting (**72%**), study activation and IRB timelines (**64%**), staffing (**61%**), and limited institutional resources (**55%**). Nearly **half** of respondents say institutional CTO priorities had significant or moderate impact on their studies, while about **one-in-five** report such impacts over intellectual property considerations.

Staffing has been a persistent challenge for many institutions since the COVID-19 pandemic. According to a survey by the SWOG Cancer Research Network, factors contributing to staffing issues included high staff turnover, which led to additional pressure on the employees who remained; limited opportunities for professional development; and a loss of morale as engagement between staff and leadership declined.[9] The staff turnover rate peaked in 2020 at 30%, and the effects are still felt today.[10]

Institutional Challenges Impacting IITs



"The pandemic and its accompanying 'great resignation' forced us to focus on ways to motivate our employees and prioritize work-life balance. We now possess tools to allow staff to work efficiently at home that didn't exist prior to the pandemic, and we have chosen to accept that. While having staff on site may be a benefit in some ways, allowing the flexibility for staff to work the way they want to as long as their position allows it is more important than any downsides to remote work."

Darlene Kitterman, MBA
University of Illinois Cancer Center

EXTERNAL CHALLENGES

Investigators seeking external funding support can face significant challenges stemming from misalignment with funder priorities. Some funders offer assistance to investigators by disclosing their areas of interest and providing convenient portals for the submission of IIT requests for support. Nevertheless, funding opportunities are competitive. **More than two-thirds** of HCRN investigators report moderate to significant challenges related to funder priorities. In addition, many investigators have been negatively impacted by competing national studies, changes in standard of care, and diminished relevance of their research proposals.

HCRN seeks to address these challenges by supporting the collaborative development of research proposals through our clinical trial working groups and facilitating regular engagement between our members and companies that are funding IITs. HCRN working groups also provide expanded opportunities for cross-institutional collaboration and mentorship.

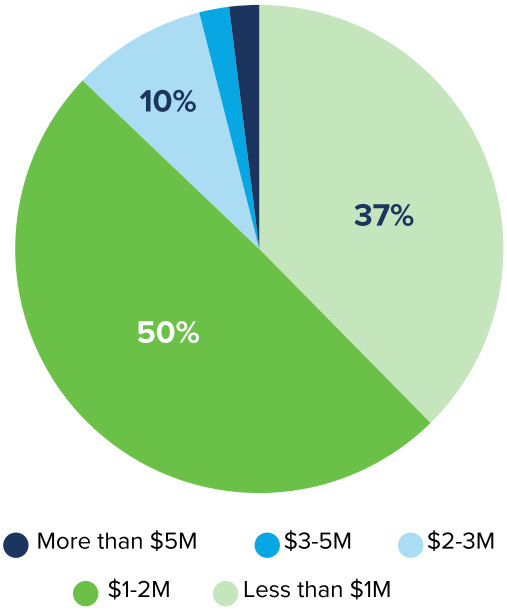
"Mentorship from Dr. Rana Mckay, along with the opportunity to collaborate with the esteemed group of GU oncologists in the HCRN working group, significantly strengthened my trial proposal and contributed to its approval."

Karie Runcie, MD
Columbia University

FUNDING CHALLENGES

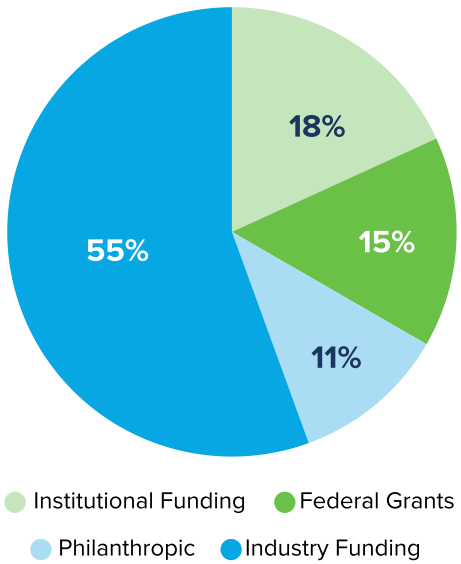
The most significant challenge for sponsor-investigators is securing adequate funding for their IITs. Given the complexity of clinical trials, IITs often require sizable budgets. **More than one-third** of respondents have average budgets less than $1 million and **roughly half** of HCRN investigators report average IIT study budgets ranging between $1-2 million. The remaining **13%** have average IIT budgets exceeding $2 million.

Average Budget for Funded IITs



Across the HCRN network, investigators rely heavily on industry for IIT support, with **55%** of funding provided by companies. Additional funding for IITs comes from institutional support (**18%**), federal grants (**15%**), and philanthropic sources (**11%**).

Average Sources of Funding for IITs



More than **80%** of HCRN investigators identified difficulty in attracting industry funders as a moderate or significant challenge. Even when a funding source is identified, it is often not sufficient to cover all study costs. **74%** of HCRN investigators identified inadequate funding as a moderate to significant impact on their studies; and **61%** said limited access to grant opportunities is also a challenge. Finally, about **half of HCRN investigators** said their studies are impacted by a lack of institutional support.

At the time of this report's publication, we are keenly aware of the additional challenges facing investigators and institutions related to the impact of potential cuts in federal funding. Additionally, we are mindful of the present uncertainty around the impact of tariffs on the pharmaceutical industry's interest in funding IITs. This report does not speculate on how these developments will impact the future of IITs or the cost of conducting research, but we recognize the need for meaningful solutions to help investigators secure the funding needed to conduct critical investigator-initiated studies.

KEY TAKEAWAYS

80%
of investigators identify moderate to significant challenges attracting industry funding

72%
of investigators strongly agree IITs are a catalyst for early-career development

58%
of investigators have participated in research that led to local changes in care, national treatment guideline changes, or new drug registrations

The Future of IITs

Despite the challenges described in this report, HCRN investigators are encouraged by the advent of new technologies and trends that show great promise – and commensurate logistical and operational hurdles – as the industry moves more deeply into an era driven by large data sets and small patient populations. Budget constraints may necessitate smaller studies that complete enrollment faster.

Further, the emergence of cellular therapy, radiopharmaceuticals, antibody drug conjugates, and AI, among other developments, has opened a wide range of potential new paths for IIT development.

> "The convergence of highly effective therapeutics and new technologies is creating a watershed moment to redefine the care of several different tumor types through well designed and efficiently executed clinical trials. Through the integration of circulating tumor DNA and artificial intelligence-based prognostic models, we are rapidly moving closer to our goal of individualizing care."

Matthew Galsky, MD, Icahn School of Medicine at Mount Sinai

Respondents rated the importance of several trends in oncology research. The following order represents the percent of survey respondents who identified these as "**very important**" trends.

60% Biomarker-based studies that address unmet needs for population subsets

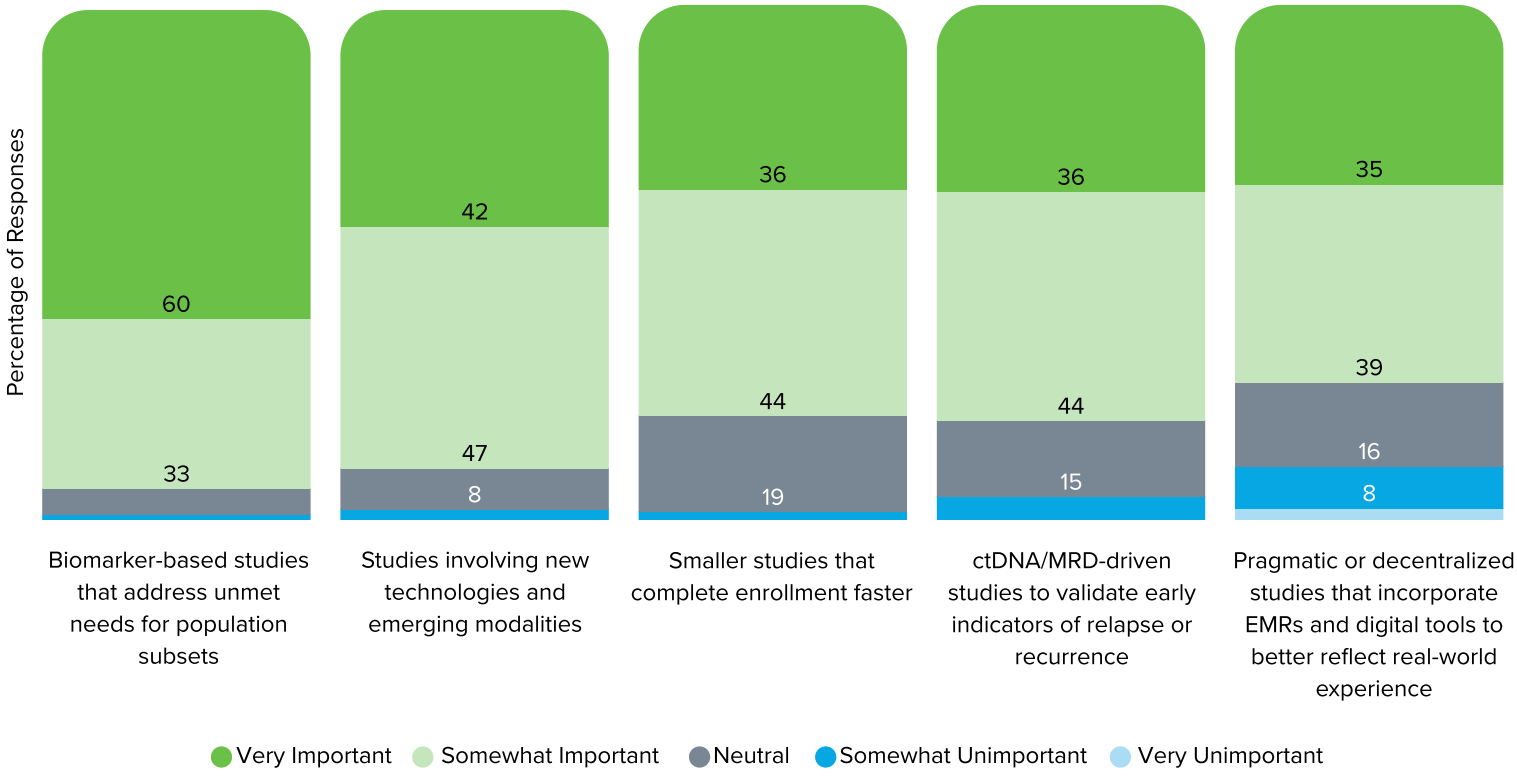
42% Studies involving new technologies and emerging modalities

36% ctDNA/MRD-driven studies to validate early indicators of relapse or recurrence

36% Smaller studies that complete enrollment faster

35% Pragmatic or decentralized studies that incorporate EMRs and digital tools to better reflect real-world experience

Importance of Oncology Research Trends



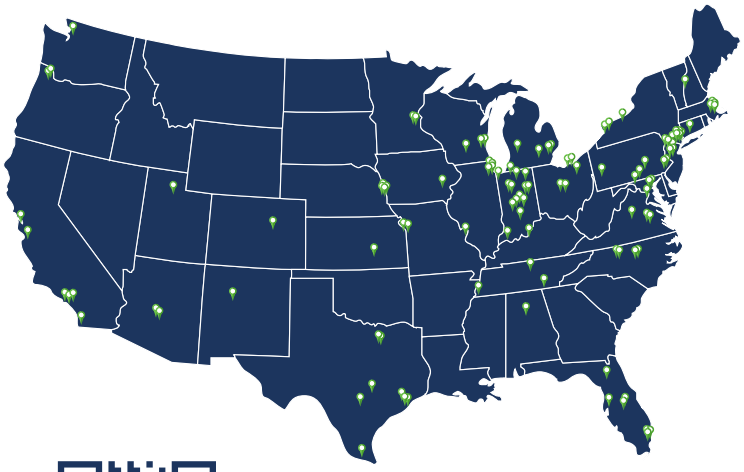
The IIT landscape, like oncology research in general, is continuously evolving. While investigators adapt to new opportunities, some difficulties that emerged during the COVID-19 pandemic persist today. We believe creative approaches that involve effective collaboration between investigators, institutions, funders, and organizations like HCRN will be **key to the future success of multi-center IITs.**

"Organizations like the Hoosier Cancer Research Network play an absolutely vital role in the conduct of investigator-initiated clinical trials, in particular those involving multiple cancer centers. HCRN's expertise and ability to link the differing clinical trial organizations across different cancer centers to generate the highest quality clinical trial data is essential in providing access to cutting-edge clinical research from a single center to a much larger patient population served by multi-center trials."

Kelvin P. Lee, MD, Director of the Indiana University Melvin and Bren Simon Comprehensive Cancer Center

Hoosier Cancer Research Network

Hoosier Cancer Research Network (HCRN), formerly known as Hoosier Oncology Group, was founded in 1984 to support cancer clinical trials led by Indiana University researchers and made available to cancer patients at community cancer centers across the state. HCRN steadily grew its footprint to include other academic centers, and in 2007, HCRN became a nonprofit, tax-exempt organization with the purpose of developing and conducting investigator-initiated oncology research. Today, HCRN supports a nationwide network that includes more than 60 academic institutions and 40 community health systems, with more than 500 investigators participating across 10 disease-specific clinical trial working groups.



www.hoosiercancer.org

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