Temporal Trends in Biomarker Utilization Across 24,000+ Immuno-Oncology Trials

Fahad Benthani, Samik Upadhaya, Cynthia L. Neben, Kellie R. McDonald, Alicia Y. Zhou
Cancer Research Institute, New York, NY

Abstract #6519

Introduction

Immuno-oncology (IO) has reshaped cancer treatment over the past decade, with checkpoint inhibitors leading a wave of clinical development that has produced over 150 U.S. Food and Drug Administration (FDA) approvals since 2011. Biomarkers like PD-(L)1, tumor mutational burden, and microsatellite instability are central to this success, helping identify which patients are most likely to benefit. As the field expands beyond the checkpoint era, understanding how biomarker-informed trial design is evolving alongside therapeutic innovation is critical for optimizing future development strategies and improving patient outcomes.

Context	Gap
IO clinical trials have grown exponentially, now exceeding 24,000 globally.	No comprehensive, longitudinal analysis of how biomarker strategies are evolving across the IO trial landscape.
Biomarkers are important for patient selection, treatment monitoring, and precision medicine.	Indication-specific differences in biomarker adoption remain poorly characterized.
The IO pipeline has expanded beyond checkpoint inhibitors into cell therapies, cancer vaccines, and bispecific antibodies.	It is unclear whether biomarker development is keeping pace with newer modalities.

Objective: Map temporal trends in IO clinical trial activity and biomarker usage across therapeutic modalities, cancer types, and trial phases using a comprehensive global database.

Methods

We curated a database of over 24,000 interventional IO clinical trials from GlobalData (data cutoff: June 18, 2025), extracting therapeutic modality, molecular targets, cancer indication, trial phase, sponsor type, and biomarker data. All entries were manually curated by CRI to resolve inconsistencies in how trials, targets, and biomarkers are labeled across source records.

- **Dataset:** 24,204 interventional IO clinical trials
- **Biomarkers analyzed:** 9,849 unique biomarkers
- **Biomarker classification:** By molecular type (protein, cell, nucleic acid, metabolite), functional role (patient selection, treatment monitoring, or both), and indication-specific usage patterns
- **Temporal analysis:** Trial start date used to assess year-over-year trends in trial initiation and biomarker adoption (2012–2024). Trials with start dates in 2025 were captured in the database but excluded from year-over-year analyses to avoid bias from a partial year.
- **Comparisons:** Solid vs. hematologic malignancies; indication-level; phase-level

References
Benthani F, Upadhaya S, Zhou A. Cancer cell therapies: global clinical trial trends and emerging directions. *Nat Rev Drug Discov* 2025;24:898–899.

Results

Figure 1. IO Clinical Trial Starts Grew Rapidly for a Decade Before Slowing

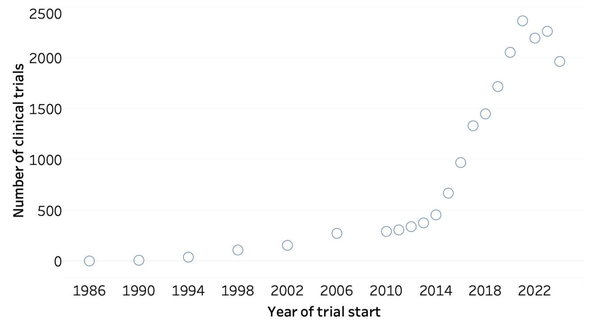


Figure 1a

CRI's database captured 24,204 IO clinical trials. Trial initiation grew exponentially from the mid-2000s, peaking around 2021 before slowing in recent years (Fig. 1a).

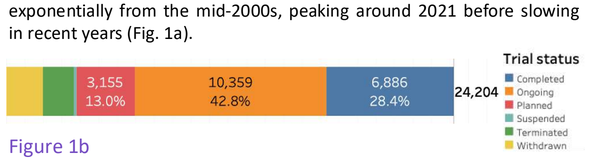


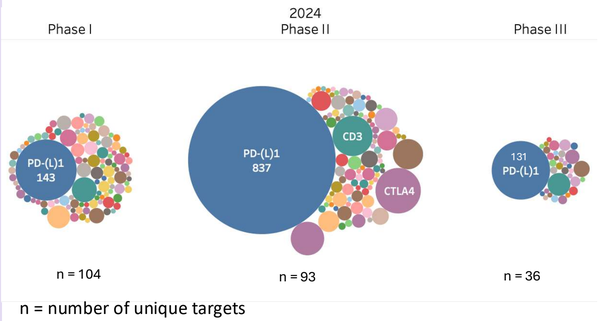
Figure 1b

Among trials started through 2024, 42.8% (10,359) were ongoing, 28.4% (6,886) were completed, and 13.0% (3,155) were terminated, with smaller proportions suspended, withdrawn, or planned (Fig. 1b).

Figure 1c

The majority were Phase II, followed by Phase I and Phase III (Fig. 1c). **Together, these data point to a field that was no longer growing as quickly but was instead focused on moving the most promising treatments forward.**

Figure 2. PD-(L)1 Dominates Late-Stage IO Clinical Trials



n = number of unique targets

Figure 2a

Results

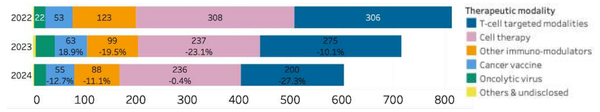


Figure 2b

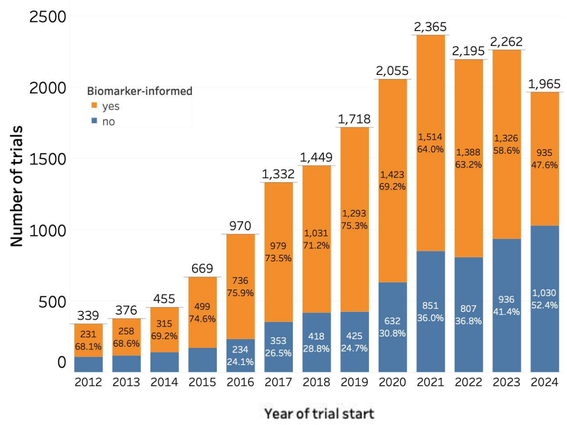
Immune checkpoint PD-(L)1 was the most common target at every stage, and its dominance grew as trials progressed (Fig. 2a). In Phase III, only a handful of targets remained alongside it. PD-(L)1's outsized late-stage presence likely reflects both its longer head start as one of the earliest IO targets and its demonstrated efficacy across multiple cancer types. As a result, few non-PD-(L)1 targets had reached Phase III, which could leave patients with limited alternatives should resistance to current checkpoint inhibitors grow.

Phase I trial starts declined across most treatment types between 2022 and 2024 (Fig. 2b):

- T-cell targeted modalities, the largest category, saw the steepest decline.
- Cell therapies and other immuno-modulators also trended downward.
- Cancer vaccines and oncolytic viruses grew in 2023 before reversing in 2024.

By 2024, every category had fewer Phase I starts than in 2022, a broad slowdown that may reduce the flow of new candidates into later-stage trials.

Figure 3. Fewer New Trials Are Using Biomarkers

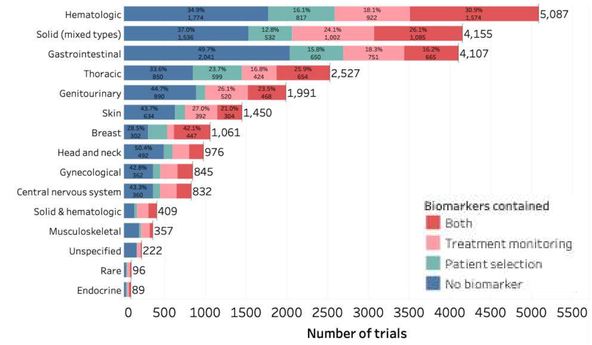


The overall share of new IO trials using at least one biomarker had been declining for years. After peaking at 75.9% in 2016, the rate fell steadily, and in 2024 fewer than half of new trials (47.6%) included a biomarker, the lowest level observed in over a decade (Fig. 3).

Notably, even as the absolute number of trials grew substantially between 2016 and 2021, the proportion using biomarkers declined, demonstrating biomarker-free trials were growing faster than biomarker-informed ones. **This widening gap raises the question of whether newer treatment approaches are outpacing the development of companion biomarkers to guide their use.**

Results

Figure 4. Biomarker Use Varies Widely Between Cancer Types



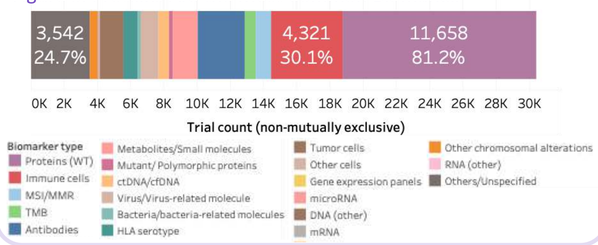
CRI's database spanned a wide range of cancer types, with hematologic, mixed solid, and gastrointestinal (GI) cancers as the largest categories by trial volume. Biomarker use varied considerably across indications (Fig. 4). Hematologic cancers led adoption at 65.1%, with 30.9% using biomarkers for both patient selection and monitoring. Among solid tumors, thoracic cancers had the highest adoption (66.4%), while GI cancers, despite the largest trial volume, used no biomarker in nearly half their trials (49.7%).

Across all biomarker-informed trials (Fig. 5):

- Proteins (wild-type) dominated at 81.2%, with MSI/MMR (30.1%) and immune cells (24.7%) also commonly used.
- Metabolites/small molecules (19.6%), TMB, ctDNA/cfDNA, and mutant proteins accounted for smaller shares.

Together, these patterns likely reflect how well-characterized each cancer's biology is and the availability of validated markers for routine trial use.

Figure 5. Proteins Are the Most Common Biomarker



Conclusions

- The IO pipeline is consolidating, shifting from broad exploration to focused development. Late-stage development remains concentrated around PD-(L)1, with few alternatives reaching Phase III.
- Biomarker use varies by cancer type. Hematologic and respiratory cancers lead; GI cancers lag.
- Biomarker use fell below 50% in 2024 for the first time in over a decade, with biomarker-free trials now outpacing biomarker-informed ones.
- **Overall**: Biomarker development is not keeping pace with IO therapy diversification, an opportunity to better align future trial design with the patients most likely to benefit.