MRD as a Primary Endpoint: The Hype Outpaces the Data

Minimal Residual Disease (MRD), an endpoint unique in liquid cancer, is frequently cited as a promising endpoint in drug development. Regulatory agencies, including the FDA, now accept MRD-negativity as a surrogate for long-term outcomes and accelerated approvals in certain cases, and its correlation with improved progression-free survival (PFS) is well documented. While industry interest is high, **current clinical trial activity tells a different story:**

- **Only one FDA-approved therapy—Carvykti (2024)—**has used MRD as a **primary endpoint** (partially based on the NCT04133636 Phase 2 trial).
- Only **four trials with MRD as a primary endpoint** have been part of discontinued clinical programs, reflecting low usage rather than strong endorsement or rejection.
- Across oncology, **just 22 active, interventional, industry-led, FDA-track trials** use MRD as **a primary endpoint; ~55%** are in **Phase 2.**
- Compare this to **200+ active Phase 2 trials** in hematologic cancers which continue to rely on **ORR or CRR** as primary endpoints. Even if we expand the parameters to the **secondary** setting**, only around 50** among those employ MRD as an endpoint.
- Of the **five currently active Phase 3 trials** using MRD as primary, **two include PFS as a co-primary,** underscoring lingering regulatory caution.

Despite growing attention, MRD has **not yet achieved broad adoption as a decision-driving endpoint, as it is still mostly employed as a secondary consideration in clinical trial design**. Reasons likely include **enrollment challenges**, such as the need to identify and consistently measure MRD-negative patients, which often requires specialized assays and frequent sampling not uniformly available across trial sites.

Operational complexity is another factor, as MRD testing typically involves high-sensitivity techniques like next-generation sequencing or flow cytometry, which can vary in accuracy, standardization, and turnaround time—introducing logistical and protocol-related burdens.

Lastly, there's a **lack of regulatory precedent** for MRD as a standalone efficacy measure: while the FDA has acknowledged its utility in certain accelerated approval contexts, the broader regulatory community remains cautious, often requiring co-primary endpoints (e.g., progression-free survival) or post-hoc validation, which dampens sponsor confidence in relying solely on MRD.

Intelligencia AI: How We Fit Into the Equation

We help sponsors bridge the gap between potential and practice by:

- Benchmarking MRD usage across indication, phase and sponsor, so teams can understand how their trial strategies align—or diverge—from industry norms and regulatory expectations
- Analyzing historical success and design patterns, helping sponsors identify what has worked in the past and avoid common pitfalls when considering MRD as a primary endpoint
- Leveraging our data and our technology to inform when—and whether—MRD should be prioritized (via custom analytics)

MRD may be trending in headlines and industry buzz, but the data tells a different story and signals caution. Successful adoption will depend on targeted, evidence-backed design strategy.