White paper

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Oncology clinical trials

Optimizing next-generation sequencing for precision oncology trials

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In cancer, precision medicine uses specific information about a patient's tumor to help diagnose, plan or evaluate treatment, or make a prognosis. This targeted approach is transforming cancer treatment by tailoring therapies to individual patients through precision oncology therapeutic development. An integral part of this approach is biomarker testing, which is becoming the 'standard of care' at many hospitals and cancer centers, allowing physicians to select the optimal treatment for each patient. However, the field is still not without its challenges, such as patient recruitment, tissue sample limitations, and quick turnaround time of the biopsy results.

Next-generation sequencing (NGS) solutions have seen promising new advancements that enable sponsors to overcome these obstacles by decentralizing trials, enhancing patient access and diversity, improving tissue-saving practices, and easing common logistical hurdles. Efficient, on-site NGS testing reduces delays and risks associated with send-out testing, creating the ability to run more efficient trial timelines. Thermo Fisher Scientific's Ion Torrent™ Genexus™ System* exemplifies these capabilities, supporting global expansion and accessible testing, and offering innovative NGS solutions for precision oncology.

Precision medicine defined

Precision medicine uses information about variations and mutations in a person's genes or proteins (biomarkers) to diagnose and treat disease. In cancer, precision medicine leverages biomarkers and other relevant information about a patient's tumor to help diagnose, plan and evaluate treatment, or make a prognosis. When more is known about the identity and mechanism of the cancer, targeted agents can be used as therapies, resulting in better outcomes for many cancer patients[1].

1. **American Cancer Society. "Precision Medicine." Cancer.org. https://www.cancer.org/cancer/managing-cancer/treatment-types/precision-medicine.html.**

The state of precision oncology trials

Precision oncology is the new frontier in therapeutic development. Recent growth within the field presents a wealth of opportunities for sponsors, as it has been valued[1] at $130 billion in 2023 and is projected to reach $364 billion by 2035. Of the more than 10,000 oncology clinical trials initiated between 2019 and 2023, about 30% focused on precision oncology, reflecting its increasing prominence. This surge has driven substantial improvements in patient outcomes, allowing for more targeted and effective treatments that go beyond the more untargeted therapies of the past.

Despite these advancements, the field still faces challenges that sponsors will need to overcome to be successful. Some of these challenges include patient recruitment and retention, complex tissue sampling logistics, and long turnaround times for testing. NGS is a commonly used tool in precision medicine and, when used strategically, can aid in addressing many of these common challenges. By broadly assessing genetic mutations and biomarkers in a patient's tumor, NGS can facilitate faster and more accurate patient enrollment in biomarker-driven trials. Consequently, this approach may lead to better outcomes for patients, as therapies are tailored to the specific characteristics of their cancer, enabling the likelihood of successful treatment.

Ultimately, success in precision oncology is supported when sponsors utilize the right, innovative NGS solutions. Read on to discover the strategic approaches for leveraging NGS that drive success in precision oncology therapeutics development.

The role of NGS in oncology biomarker-driven trials

A precision medicine approach to cancer therapeutics is a biomarker-driven strategy with a laser focus on delivering therapies to the right patients at the right time. This is why predictive biomarker testing has become the basis for selecting appropriate precision therapies for cancer patients. It has helped to transform cancer treatment, which has evolved dramatically over the past 25 years.

NGS enables precision oncology by revealing the genetic identity of a tumor. This is crucial because even when two patients have the same type of cancer, the genetic makeup and mechanisms of their cancers can vary. Understanding the genetics of a patient's tumor often provides insight into the cancer's mechanisms, enabling researchers to develop more effective, targeted therapies compared to more generalized solutions. NGS allows for the testing of many potential mutations simultaneously, making it easier to understand an individual's cancer and thus

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* In the US; For Research Use Only. Not for use in diagnostic procedures. Dx status varies per region.

NGS in action

Clinical trials such as PROFILE 1014 are examples of landmark trials in the use of NGS in precision oncology. This trial revolved around the treatment of ALK-positive non-small cell lung cancer (NSCLC). The trial demonstrated that crizotinib significantly improved progression-free survival and objective response rate compared to chemotherapy[1]. This trial, among others, was pivotal in shifting the paradigm to biomarker-driven treatment approaches in NSCLC, underscoring the importance of identifying genetic mutations to personalize treatment. Evidence like this supported the incorporation of molecular testing into clinical practice.

Organizations such as the National Comprehensive Cancer Network (NCCN) recommend that molecular testing should be conducted as part of broad molecular profiling, defined as testing that identifies all biomarkers specified in NCCN Guidelines for NSCLC[2].

1. **Solomon BJ, Mok T, Kim DW, et al. "First-Line Crizotinib versus Chemotherapy in ALK-Positive Lung Cancer." N Engl J Med. 2014;371:2167-2177. DOI: 10.1056/NEJMoa1408440.**
2. **NCCN Guidelines Version 11.2024 Non-Small Cell Lung Cancer**

develop individualized therapies that save lives. NGS also allows drug developers to discover new biomarkers, screen patients for selection in clinical trials, develop companion diagnostics, and develop personalized treatment plans.

Adopting an appropriate NGS solution can help sponsors and pharmaceutical companies address many obstacles in therapeutic development. However, not all NGS solutions are created equal. Choosing the right solution can aid in mitigating common challenges in oncology therapeutic development.

Enhancing patient recruitment through decentralization

One of the initial challenges a sponsor may encounter when developing precision oncology therapeutics is patient identification, access and recruitment. Finding the right patients for these trials can be like finding a needle in a haystack. Addressing this issue is even more critical given that over 50% of lung cancer patients in the U.S. do not receive the optimal treatment[2]. Patients are often lost throughout the testing journey, particularly due to complications such as tissue quality and turnaround time. Nearly 30% of these patients are lost because of suboptimal testing technology, which can result from inconclusive results, false negatives or prolonged turnaround times [2].

While addressing these issues, sponsors must also ensure the enrollment of diverse populations in their studies. Diversity in clinical trials allows the findings to be applicable to broader populations and this is particularly important for biomarker-driven clinical trials. Because biomarkers can vary across different populations, diverse participation in biomarker-driven trials prevents disparities, thereby helping to ensure that all groups have access to the benefits of precision medicine. In the U.S., drug developers should consider the disparity in access between white patients and patients in the racial minority when planning recruitment strategies. Globally, there is often difficulty reaching patients in rural areas and emerging countries. Addressing these issues head-on requires sponsors to maintain a patient-centric approach and implement optimal technology to reduce patient burden.

Decentralization is one approach that can be used to ease some of the most common patient hurdles. Incorporating digital and decentralized elements into a trial often makes participation more feasible for potential patients. Accessible and widespread use of NGS technology is an effective tool in accomplishing this. When NGS testing technology is available in-house, it enables sites of all sizes to test biopsy samples, increasing the range of these trials and enhancing the team's ability to enroll the right patients.

Subsequently, on-site NGS is a valuable tool when addressing disparities in biomarker testing between different demographic groups, easing challenges in enrolling diverse patient populations by extending reach to meet rural and minority groups where they are. The ability to better reach patients also aids in easing the burdens of the trial, making participation more manageable for patients who may be very ill. Time is precious for these patients. The right NGS solution allows sponsors to accelerate their programs—ultimately getting patients to treatment earlier and keeping patient-centricity at the center of their trial strategy.

Enable tissue-saving practices with the right NGS solution

Tissue sample limitations is another area of complexity for drug developers in precision oncology. Common problems include insufficient tissue samples for testing, inconclusive test results due to limited tissue, and high rates of failure—as much as 30%[2]—for some commonly used testing methods. These issues often result in repeat biopsies, which is challenging for patients, and some tumor types may not yield sufficient tissue for re-biopsies.

Innovative and accessible NGS solutions can alleviate these issues. Amplicon-based NGS solutions are particularly optimal for these applications due to their low input requirements, which allow the use of limited samples and enable increased test success rates, thus expanding trial eligibility and improving efficiency.

Additionally, the ability to test both liquid and tissue biopsies makes trials more accessible to patients who may not have sufficient tissue biopsies available or those who cannot undergo invasive procedures. The dual application of liquid and tissue biopsies allows for complementary insights, and by leveraging both methods, sponsors can achieve a more comprehensive understanding of tumor biology and enhanced trial enrollment.

Improving trial efficiency with accessible NGS technology

When using NGS in precision oncology studies, it is common for clinical sites to send out samples to reference labs for testing. When sites have to send samples away for testing externally, it can often take weeks[3] to get results. The increasingly global nature of precision oncology trials is exacerbating logistical challenges, such the need to cross borders, which raise the risk of samples being lost or compromised and create tighter timelines when retesting is necessary.

It should be noted that immunohistochemistry (IHC) has historically been performed in local laboratory settings, which allows for timely processing and analysis of tissue samples, making it a practical and commonly used technique in clinical diagnostics and research. NGS, in comparison, has historically not been able to be as broadly accessible, as many NGS solutions are too complex, too manual, and require expert users. Community hospitals are often overburdened and lack the expertise needed to operate a complicated workflow in-house. As the field of precision oncology continues to innovate, better ways are quickly emerging.

Recent innovations in the field have made it possible to approach NGS in a similar way to IHC. More advanced and efficient NGS solutions have the ability to:

- Reduce logistical complexities with rapid on-site testing
- Streamline workflows through automation, saving time and labor
- Test more samples successfully due to amplicon-based chemistry
- Expand patient access through ease-of-use

Accessible, easy-to-use, widespread NGS technology sets the stage for more efficient trials, enhancing the ability to decrease turnaround time and add flexibility for precision oncology studies.

Selecting the right NGS solution

The right NGS solution for the development of precision oncology therapeutics allows sponsors to meet the needs of the trial landscape today. With it, sponsors are able to:

- Ease patient identification and access through decentralization
- Have more efficient, tissue-saving practices
- Become increasingly global while enabling quick turnaround times
- Create the groundwork needed for efficient timelines
- Identify more patients eligible for treatment

The PPD™ clinical research business of Thermo Fisher Scientific has brought precision medicine capabilities to community sites, empowering them to be an end-to-end solution for our clients. We do so with innovations like Oncomine Solutions, our in-house, high-speed genomic profiling solutions. Oncomine Solutions enable sponsors to solve many of the most common issues faced by precision medicine therapeutics development while allowing for elevated global insights into genomic profiling for better study feasibility and site strategy.

Several of our Oncomine Solutions have a dual application for tissue and liquid biopsies, allowing sponsors to use both sample types to streamline testing processes. Low sample input requirements, enabled by amplicon-based chemistry, maximize tissue retention, with a more than 95% success rate even with input as low as 10 ng in as little as 48 hours. This can be particularly helpful for companion diagnostics (CDx) development, as NGS plays a critical role in CDx to support drug submission and approval. The Oncomine Dx Target Test** was the first distributable NGS-based CDx solution approved by the U.S. Food and Drug Administration in 2017. Since this approval,

** For *In Vitro* Dagnostic Use.

we have partnered with 14 pharma companies and expanded its indication to 20 therapies on the label across 19 countries and 11 CDx biomarkers.

Our team is constantly innovating in genomic profiling to advance further adoption of NGS. We are dedicated to driving the modernization of clinical trials by creating and implementing new decentralized solutions. Oncomine Solutions are used at more than 1,000 sites globally, aligning with our clinical development efforts worldwide, including in emerging countries, to support trials in various regions. Our Oncomine NGS Solutions allow sites to test patients locally without sending out samples and can deliver molecular results in as little as 24 to 72 hours, alongside IHC results. This enables the determination of the most appropriate clinical trial for the patient in a timely manner.

Our global reach and proven history in supporting drug submissions and approvals empower our teams with the knowledge needed to lead in NGS innovation within precision oncology. Over the past five years, we have conducted more than 700 oncology studies, and the PPD clinical research business of Thermo Fisher Scientific offers complete end-to-end solutions for clinical trials. From recruitment to companion diagnostic development, submission applications to commercial launch, our broad capabilities support your needs.

Endnotes

1. Roots Analysis. "Oncology Precision Medicine Market." https://www.rootsanalysis.com/reports/oncology-precision-medicine-market.html. Accessed October 17, 2023.
2. Sadik H, et al. Impact of Clinical Practice Gaps on the Implementation of Personalized Medicine in Advanced Non–Small-Cell Lung Cancer. JCO Precis Oncol. 2022;6:e2200246. doi:10.1200/PO.22.00246.
3. Roberts NJ, Espirito JL, Chen L, et al. Biomarker testing and tissue journey among patients with metastatic non-small cell lung cancer receiving first-line therapy in The US Oncology Network. Lung Cancer. 2022. https://www.lungcancerjournal.info/article/S0169-5002(22)00373-7/fulltext. Accessed October 17, 2023.

Enhance your precision oncology trial by optimizing NGS solution

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