TruSight™ Oncology 500: Enabling Comprehensive Genomic Profiling for Every Laboratory

The next step in precision medicine lies in decentralizing comprehensive biomarker testing

In the fight against cancer, the future lies in immuno-oncology. This powerful treatment strategy bolsters the immune system's ability to target and destroy cancerous cells – but despite its promise, not all patients who undergo this treatment will benefit. Why? Because not all tumors respond equally to immunotherapy. The solution lies in leveraging biomarkers that can assist in distinguishing responders from non-responders to thereby recommend appropriate immuno-oncology approaches for patients who are likely to benefit.

Key immuno-oncology biomarkers include tumor mutational burden (TMB), which measures the number of nonsynonymous mutations within the coding region of a tumor genome as a surrogate of the likelihood of neoantigen presentation by the tumor, and microsatellite instability (MSI), a Food and Drug Administration (FDA)-approved pan-cancer biomarker that can identify tumors for treatment with immune checkpoint inhibitors. When combined with detailed mutation analysis, these markers contribute to an unprecedented level of personalization.

The personal touch

Biomarkers can yield clues to tailor the best treatment for each individual – but biomarker testing carries challenges of its own. In lung cancer, for instance, pathologists often apply a battery of iterative single-gene tests: *EGFR, ALK, ROS*, and more. And, as molecular pathology becomes increasingly advanced, multiple biomarkers are needed – TMB, MSI, and fusions, including *NTRK* with the added complexity of multiple unknown fusion partners. Guidelines from the European Society for Medical Oncology (ESMO) now include TMB in the recommended biomarker tests for non-small cell lung cancer (1). But testing each of these markers sequentially requires additional time and money. It also calls for a significant amount of tissue, which presents a challenge for most lung cancer biopsies.

Sequential testing is not the only – or the optimal – approach to personalized lung cancer treatment. Comprehensive genomic profiling (CGP) through the use of next-generation sequencing (NGS) can achieve the same results and more – while taking less time and using less precious tissue. Performing NGS on limited tumor material also can minimize the impact of intratumoral heterogeneity.

NGS is being used to examine multiple biomarkers simultaneously, allowing users to identify potential driver alterations and treat patients in accordance with the characteristics their tumors display. NGS is key to the advancement of CGP, but there remains a need for a commercially available, standardized solution that enables laboratories to perform their CGP testing on-site.

Table 1. CGP content consolidates multiple assays into one

TruSight Oncology 500		
DNA	*Key variant types*	*Example biomarkers*
	SNVs	KRAS G12D
	Indels	EGFR exon 19
	CNVs*	BRAF V600E
	Key biomarkers	*Example biomarkers*
	MSI	MSI-high
	TMB	TMB-high
TruSight Tumor 170		
RNA†	*Key variant types*	*Example biomarkers*
	Fusions	ALK ROS RET NTRK
	Splice variants	Met exon 14

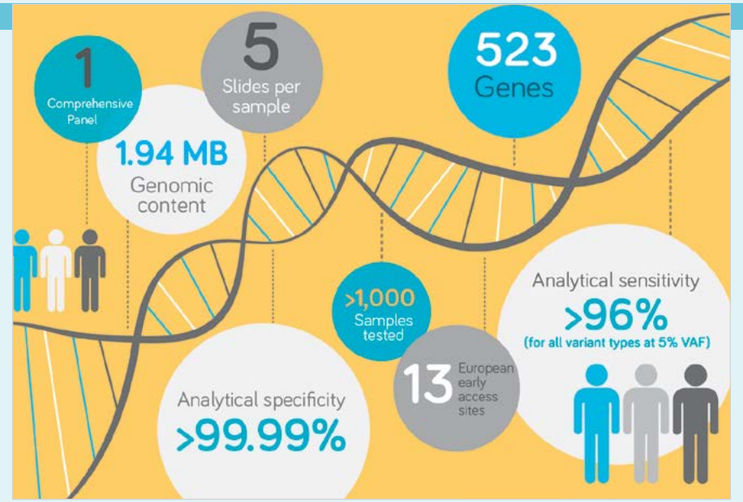
**CNV calling will be available in 2019 with an Illumina software upgrade.*

† The products to evaluate DNA and RNA variants consist of the TruSight™ Oncology 500 DNA panel and the TruSight™ Tumor 170 RNA panel (PN: 20028215, 20028216, 20032626 & 20032627).

Enabling CGP Using TruSight Oncology 500

TruSight Oncology 500 (TSO500) is currently on the market as a research use only (RUO) product that analyzes hundreds of current and emerging cancer-related biomarkers (see Table 1). These include key immunotherapy markers like TMB and MSI, which TSO500 examines using 1.94 MB of genomic content, a tumor-only workflow, and sophisticated software algorithms to yield results similar to whole exome sequencing. When bundled with TruSight™ Tumor 170 (TST170), this DNA + RNA assay† targets 523 genes to also assess small variants, splice variants, and fusions, with hybrid-capture chemistry that ensures high sensitivity and fewer sample dropouts.

TSO500 launched in January 2019 following the completion of an early access project in collaboration with 13 leading European cancer centers.



TruSight™ Oncology 500 – By the Numbers

- University of Birmingham, UK
- Institute of Pathology, University Hospital Cologne, Germany
- Institute of Pathology Erlangen, Germany
- Heidelberg Institute of Pathology, Germany
- Technical University of Munich, Germany
- Institut Gustave Roussy, France
- Radboud University Medical Center, The Netherlands
- Uppsala University, Sweden
- Jessa Hospital Hasselt/University Hospital Gent, Belgium
- University Hospital Lausanne (CHUV), Switzerland
- Hospital 12 de Octubre, CNIO & CIBERONC, Spain
- European Institute of Oncology - IEO, Italy
- Medical University Vienna/CeMM, Austria

Notably, of the 13 participating institutions, 11 participated in an inter-laboratory reproducibility assessment. This inter-laboratory reproducibility assessment demonstrates the robustness of TSO500 with observed Standard Deviation (SD) in the range of 1.5 for TMB values around 5 mut/Mb and near 3.0 for TMB values ranging from 30–80 mut/Mb (data to be published in the coming months). The study provided proof-of-concept that this assay can be reliably performed in decentralized laboratories. To scale for future worldwide deployment, users need a commercially available solution – and the minimal variation between sites in this broad study indicates that, with TSO500, it's a feasible goal.

A promising outlook

Feedback from the TSO500 early access sites was enthusiastic. Andrew Beggs, Reader in Cancer Genetics and Surgery at the Institute of Cancer and Genomic Sciences at the University of Birmingham, presented some of his laboratory's first results during the satellite symposium at the ESMO Immuno-Oncology Congress in Geneva. Beggs stated, "TruSight Oncology 500 has a number of significant advantages. It allows us to explore tumor samples of limited scope in a much more advanced way than we've previously been able to do."

Illumina's CGP product roadmap includes CE-IVD certification, initially for TMB and subsequently for other biomarkers. Given the potential benefits of liquid biopsy, Illumina entered into a multi-year collaboration using TSO500 with the Frederick National Laboratory for Cancer Research (FNL) to further explore clinical utility (2). Because liquid biopsy is still in its infancy, it requires additional validation to more fully demonstrate clinical utility. As we move down the path to regulatory approval and future in vitro diagnostic tests, we have begun to set a pioneering standard for accurate and reproducible testing.

† The products to evaluate DNA and RNA variants consist of the TruSight™ Oncology 500 DNA panel and the TruSight™ Tumor 170 RNA panel (PN: 20028215, 20028216, & 20032627).

For Research Use Only. Not for use in diagnostic procedures.

References

1. *D Planchard et al., "Metastatic non-small cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up", Ann Oncol, 29, iv192–iv237 (2018). PMID: 30285222.*
2. *Illumina, "TruSight Oncology 500 selected to power liquid biopsy studies" (2019). Available at: https://bit.ly/2C83bzK. Accessed March 8, 2019.*

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- Andrew Beggs
University of Birmingham