OmniSeq INSIGHT

The Right Drug or the Right Trial...for Every Patient.

Intended Use & Performance Specifications

INTENDED USE

OmniSeq INSIGHT is a next generation sequencing-based in vitro diagnostic device for the detection of genomic variants, signatures, and immune gene expression in formalin-fixed paraffin-embedded (FFPE) tumor tissue. DNA is sequenced to detect small variants in the full exonic coding region of 523 genes (single and multinucleotide substitutions, insertions, deletions and indels), including genes leading to homologous recombination repair defects (HRR/HRD), copy number alterations in 59 genes (gains and losses), as well as analysis of microsatellite instability (MSI) and tumor mutational burden (TMB) genomic signatures. RNA is sequenced to detect fusions and splice variants in 55 genes, in addition to mRNA expression in 64 immune genes. The resultant information, along with PD-L1 protein expression by immunohistochemistry (IHC), is intended for use by qualified health care professionals in accordance with professional guidelines in oncology for management of patients with solid neoplasms, and is not conclusive or prescriptive for labeled use of any specific therapeutic product.

TEST PRINCIPLE

OmniSeq INSIGHT is performed exclusively as a laboratory service using DNA and RNA co-extracted from formalin-fixed, paraffin-embedded (FFPE) tumor samples. The assay employs a single nucleic acid extraction method from routine FFPE biopsy or surgical resection specimens; 40 - 100 ng of DNA and 20 - 100 ng RNA undergo library construction and hybridization-based capture of all coding exons from 523 cancer-related genes and select regions from 55 commonly rearranged genes. Using the Illumina® NovaSeq 6000 platform, hybrid capture–selected libraries are sequenced to high uniform depth (targeting >150X median coverage with >90% of exons at coverage >50X), and the sequence data is analyzed to detect genomic variants and signatures. Amplicon-based targeted next generation RNA-sequencing for digital gene expression is used to assess mRNA expression in 64 immune genes, and immunohistochemistry (IHC) is used to measure PD-L1 protein expression (SP142 or 22C3 antibodies) based on the tumor type tested.

PERFORMANCE CHARACTERISTICS

Performance characteristics were established using DNA and RNA derived from a wide range of FFPE tissue specimens harboring variants with both strong and potential clinical significance, including resections, needle core biopsies and cell blocks from fine needle aspirations. For genomic profiling, each performance study included representative variant types from each alteration class (substitutions, insertions, insertions and deletions, copy number alterations, and fusions/splice variants), in various genomic contexts across a broad selection of genes, in addition to analysis of TMB and MSI genomic signatures. The detection of genomic variants by OmniSeq INSIGHT was compared to results of other validated next generation sequencing assays to assess concordance with orthogonal methods. For immune gene expression, sequencing analytical validation studies were performed to confirm standard measurements including accuracy, sensitivity and specificity. addressed variability in nucleic acid input amounts, genomic DNA contamination of RNA, batch size and linearity of detection across all genes within a wide distribution of signal on the overall immune response signature.

Table 1. OmniSeq INSIGHT Performance Characteristics

NGS	Passing Criteria	Genes/ Loci	Marker	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
DNA-Seq	Tier I hotspots: ≥ 2% VAF Non-hotspots: ≥ 5% VAF	523	Substitutions	99%	>99%
			Insertions	96%	>99%
			Deletions	99%	>99%
	≥ 2.2x fold change; 30% tumor purity	59	Copy Number	91%	99%
	≤ 0.7x fold change; 50% tumor purity	4			
	≥ 20% tumor purity	521	TMB ≥ 10 mut/Mb	87%	88%
		130	MSI	96%	>99%
RNA-Seq		55	Fusions	93%	>99%
		2	Splice variants	89%	>99%
	≥ 20 reads	64	Immune gene expression	Not applicable	

OmniSeq INSIGHT was developed, and its performance characteristics determined by the OmniSeq, Inc. in Buffalo, NY. OmniSeq® is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) and by the New York State Clinical Laboratory Evaluation Program as qualified to perform high complexity clinical laboratory testing, including all components of OmniSeq INSIGHT. OmniSeq's CLIA certification number is located at the bottom of each report, and all registered marks are the property of OmniSeq, Inc. The genomic and immune NGS components of OmniSeq INSIGHT are laboratory developed tests that have not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that clearance or approval is not currently necessary for certain laboratory developed tests. The FDA has approved the PD-L1 IHC components of OmniSeq INSIGHT for in vitro diagnostic use. OmniSeq INSIGHT is for clinical purposes and should not be regarded as investigational or for research.