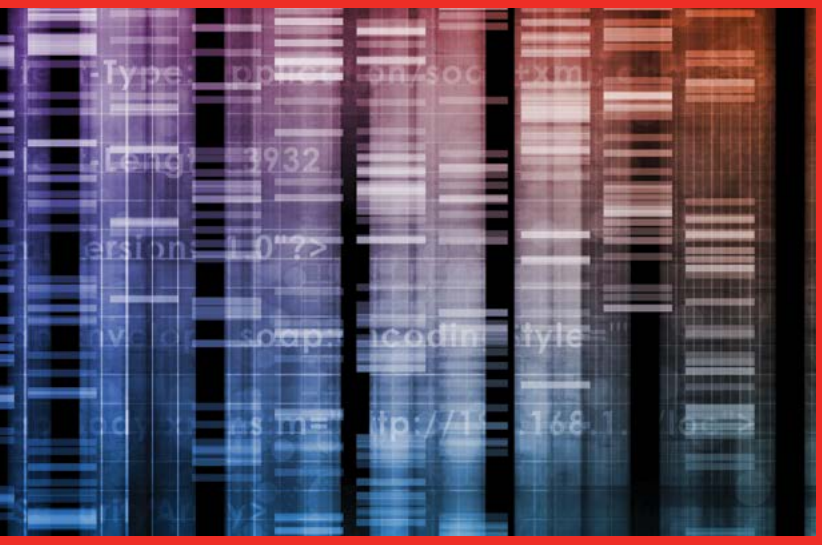
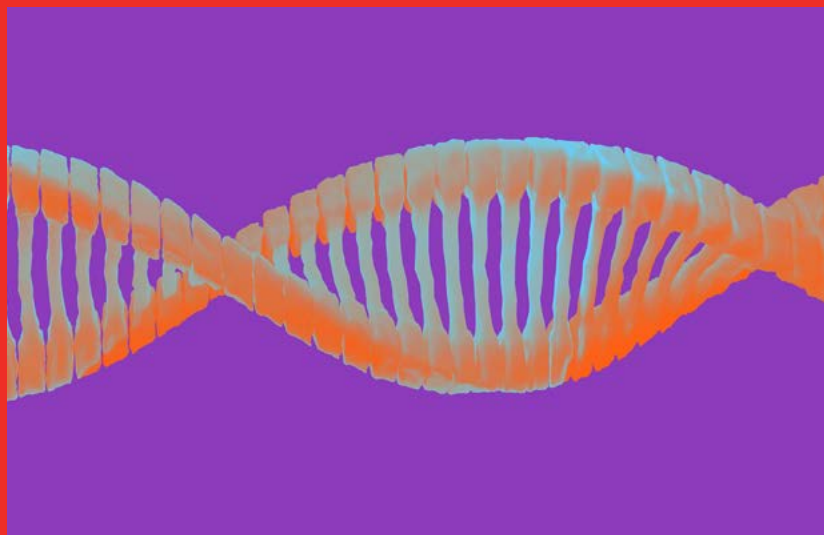
The NGS Report Decoded



Informing treatment decisions



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NGS report guide: Translating data to insights

This document walks you through a sample NGS test report and explains key sections and information. Note that not all sections will be on a single page in a typical report, and some sections may be placed on different pages[1,2]

SAMPLE MOLECULAR BIOMARKER REPORT

See pages 4 and 5 for more information on the numbered sections of this sample report

Basic Patient Information[1-7]

Patient Name XXXXX Birthdate XX/XX/XXXX Diagnosis Non–small cell lung carcinoma	Ordering Physician Dr X Medical Facility XXXXX Pathologist Dr Y	Test Solid Tumor Profile by NGS Specimen FFPE Collected on XX/XX/XXXX Received on XX/XX/XXXX Reported on XX/XX/XXXX

Biomarker Results Summary 1

Tier[1-3,6,7] 2	Biomarker[1-6] 3	Allele Frequency (VAF)[2-5] 4	Targeted Therapy[2-5] 5
I	*Biomarker 1 (exon A deletion)*	50%	Treatment X and Treatment Y are indicated as a targeted therapy for *Biomarker 1 (exon A deletion)*. Treatment Z may be contraindicated. Treatment AA is being studied in clinical trials for this biomarker.

Interpretive Summary 6

Histological Diagnosis[1,3,6,7]

Adenocarcinoma of the lung

Test Result Interpretation[2,3] 7

The *Biomarker 1 (exon A deletion)* variant is known to be oncogenic. Treatment X and Treatment Y are FDA approved for this variant in these types of cancer: NSCLC, colorectal cancer. Treatment X has a category-1 preferred recommendation for this alteration in the NCCN treatment guidelines for NSCLC and Treatment Y has a category-1 recommendation for this alteration in the NCCN treatment guidelines for NSCLC. Tumors with *Biomarker 1 (exon A deletion)* variant may develop resistance to certain treatments. Additionally, clinical studies have demonstrated that Treatment Z may be less effective for patients with this biomarker.

Pertinent Negatives[2,3] 8

No other clinically relevant molecular alterations detectable by this assay were identified. Pertinent negatives include but are not limited to the absence of X mutation, Y rearrangement, or C rearrangement.

Clinical Trials[3,4]

Biomarker 1 (exon A deletion) is associated with NCTXXXXXXXX.

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See pages 4 and 5 for more information on the numbered sections of this sample report

Detailed Interpretation[2-4] 9

Biomarker 1 (exon A deletion)	Biomarker 1 is a transmembrane receptor tyrosine kinase. Numerous variants of the gene have been identified and investigated for their role in oncogenesis and sensitivity/resistance to targeted therapy. NCCN recommends TKIs as 1L therapy in patients with NSCLC whose tumors harbor *Biomarker 1 (exon A deletion).*

Variants of Unknown Clinical Significance[1-3,5,6] 10

Gene A (XX%), *Gene B* (XX%), *Gene C* (XX%)

Test Description, Limitations, & Laboratory[1-3,6,7] 11

This NGS test is designed to detect variants present in any FFPE tissue from solid tumors. The test is designed to detect alteration types M, N, and O in a select group of genes. This test has an analytical sensitivity for detecting YY% alteration type M and YY% alteration type N in a background of non-mutated DNA sequence.

The genes tested include *Gene A, Gene B, Gene C, Biomarker 1, ...*

Laboratory Name
Address
Laboratory Director

Clinical Trials[3,4]

Biomarker 1 (exon A deletion)	NCTXXXXXXXX, A Phase 1/2 Study to Assess DRG-0001, an Oral Biomarker 1 Inhibitor, in Patients With Glioblastoma or Non-Small Cell Lung Cancer Locations: Alabama, Arizona, California...

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NGS report section descriptions

1 Biomarker Results Summary

Contains all detected potentially actionable genomic alterations with associated therapies,[3,4,8] as well as alterations NOT detected, to guide diagnostic procedures for some cancers[4,9]

Note that this may include both specific gene alterations as well as genomic signatures (eg, MSI-H, TMB). It is also possible that these two types of biomarkers will be presented in separate sections within the report[1-5,8,9]

Other names for this section may include*:

- Variants of Strong/Potential Clinical Significance[1,6,7]
- Biomarker/Genomic/CDx Associated Findings[4]
- Summary of Somatic Alterations & Associated Treatment Options[5]
- Results with Therapy Associations[2]

2 Tier

Denotes the level of clinical significance of a variant based on published literature or guidelines[2,3,8]

Tiers may or may not appear in the report and may vary depending on the laboratory, with some using their own tiering system, different from that of the National Comprehensive Cancer Network® (NCCN®)[1-4,6-9]

3 Biomarker

May be listed as a type of alteration (eg, fusion, insertion, deletion, etc.) of an altered gene[1,2,5]

Matched treatment is indicated for specific alteration types only. For example, therapy indicated for a gene fusion may not be effective for a skipping mutation in the same gene[8,10]

4 Allele Frequency (VAF)

Indicates the proportion of a variant allele in a sample[3,11]

This information may help indicate how reliable the results are. Low-frequency mutations may not be detected[1,6,7,11]

In certain situations, VAF can be used to indicate whether a variant is somatic or germline in nature[3]

Sometimes, CHIPs are detected. These are somatic mutations from a nontumor source with a VAF ≥2%. The efficacy of targeting CHIPs is unknown[4,11]

Did you know?

The amount of variant in a sample may be reported differently depending on the laboratory[2-5,8,11]

- **Tumor fraction** is the percentage of ctDNA in a sample, which can help indicate the strength of the results (eg, higher tumor fraction indicates more reliable results). If liquid biopsy is used, tumor fraction is shown as an estimate of ctDNA percentage in cfDNA[4,11]
- **Variant allele frequency (VAF)** is the fraction of abnormal alleles out of total alleles[11]
- **Copy number variant (CNV)** is a variation in the number of copies of a particular segment of DNA in the genome including insertions, deletions, and duplications[11,12]

In some cancers, mutations may be inherited. Some NGS reports may present these germline alterations in addition to somatic alterations[1,9,13]

They may provide further prognostic information. Germline alterations may also warrant testing of family members. Consider referral to a genetic counselor[13]

*Not a comprehensive list.

NGS report section descriptions (continued)

5 Targeted Therapy

May list treatments associated with the detected alteration[4,5,8]

This section may also indicate possible resistance to certain treatments[4,5,8]

Did you know?

NGS reports can help identify potential resistance mechanisms before and after 1L treatment[13]

A resistance mechanism may occur organically or as an acquired mechanism following therapy[13,14]

6 Interpretive Summary

Describes additional information relevant to the upfront results summary. It may:

- Include histological diagnosis and characterization of the tumor[2,3,8]
- Identify methodological factors impacting result interpretation[2,8]
- Give further detail on the clinically relevant molecular biomarkers detected and the related therapeutic information[3,8]
- Summarize clinical trials related to the variant detected[2,3,5]

7 Test Result Interpretation

May indicate a specific brand-name treatment if the test ordered was a CDx for that variant[2,4]

Otherwise, the unbranded molecule name is given[3-5]

8 Pertinent Negatives

May list important alterations that the patient does NOT have[2-4,8,9]

Absence of specific alterations in molecular biomarkers may also aid in treatment decisions for relevant cancer types[8]

Pertinent negatives may not be included in liquid biopsy tests from some laboratories[4,10]

9 Detailed Interpretation

Explains how the variant can lead to cancer and how it is common in the specific tumor type and patient demographic[2-4,8]

It cites relevant evidence-/consensus-based peer-reviewed practice guidelines[3,4,8]

It describes the therapeutic, predictive, and prognostic implications identified by tumor type[2-4,8]

10 Variants of Unknown Clinical Significance

Lists variants that do not have a clearly defined clinical significance at the time of reporting but may potentially be useful for screening, surveillance, or treatment selection in the future[8]

Allele frequency may also be included[5,11]

11 Test Description, Limitations, & Laboratory

Also known as Methodology, provides relevant pre-analytical, analytical, clinical, demographic, interpretive, and reporting components that can affect result interpretation[1-3,6-8]

May indicate whether the test can detect germline or somatic variants, or both[1-3,6,7,9]

May indicate if MSI or high TMB were identified[2,3]

If there were issues with the analysis, results may not be reliable and testing may need to be repeated[8,13,15]

1L, first-line; CDx, companion diagnostic; cfDNA, cell-free DNA; CHIP, clonal hematopoiesis of indeterminate potential; CNV, copy number variant; ctDNA, circulating tumor DNA; DNA, deoxyribonucleic acid; FDA, U.S. Food and Drug Administration; FFPE, formalin-fixed, paraffin-embedded; MSI, microsatellite instability; MSI-H, microsatellite instability-high; NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing; NSCLC, non–small-cell lung cancer; TKI, tyrosine kinase inhibitor; TMB, tumor mutation burden; VAF, variant allele frequency.

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Data rates may apply

Solutions start with a conversation

Take action and speak to
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