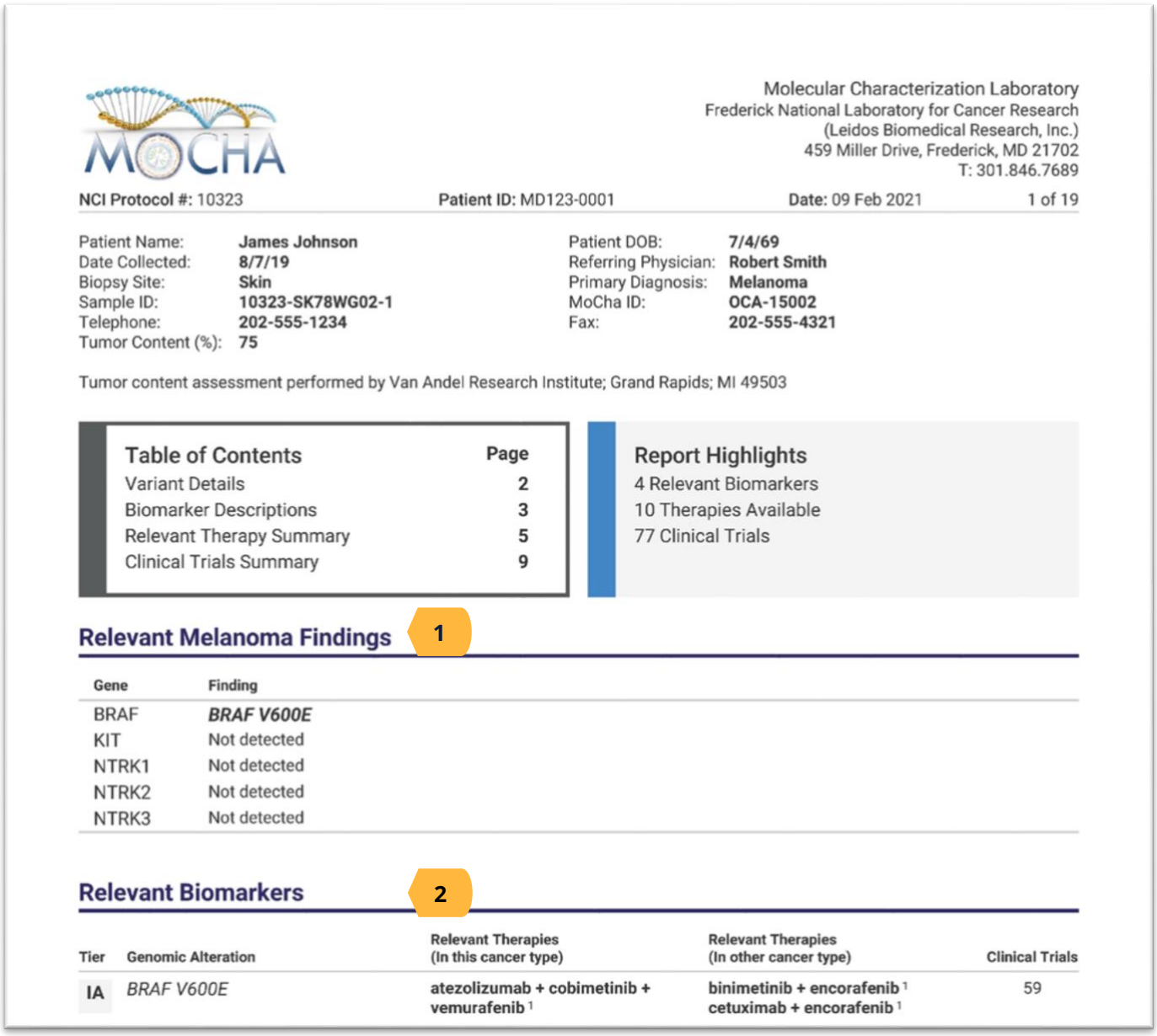
Guide to the MOCHA Solid Tumor Biomarker Report



MOCHA

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NCI Protocol #: 10323 | Patient ID: MD123-0001 | Date: 09 Feb 2021 | 1 of 19

Patient Name:	James Johnson	Patient DOB:	7/4/69
Date Collected:	8/7/19	Referring Physician:	Robert Smith
Biopsy Site:	Skin	Primary Diagnosis:	Melanoma
Sample ID:	10323-SK78WG02-1	MoCha ID:	OCA-15002
Telephone:	202-555-1234	Fax:	202-555-4321
Tumor Content (%):	75		

Tumor content assessment performed by Van Andel Research Institute; Grand Rapids; MI 49503

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Relevant Melanoma Findings 1

Gene	Finding
BRAF	*BRAF V600E*
KIT	Not detected
NTRK1	Not detected
NTRK2	Not detected
NTRK3	Not detected

Relevant Biomarkers 2

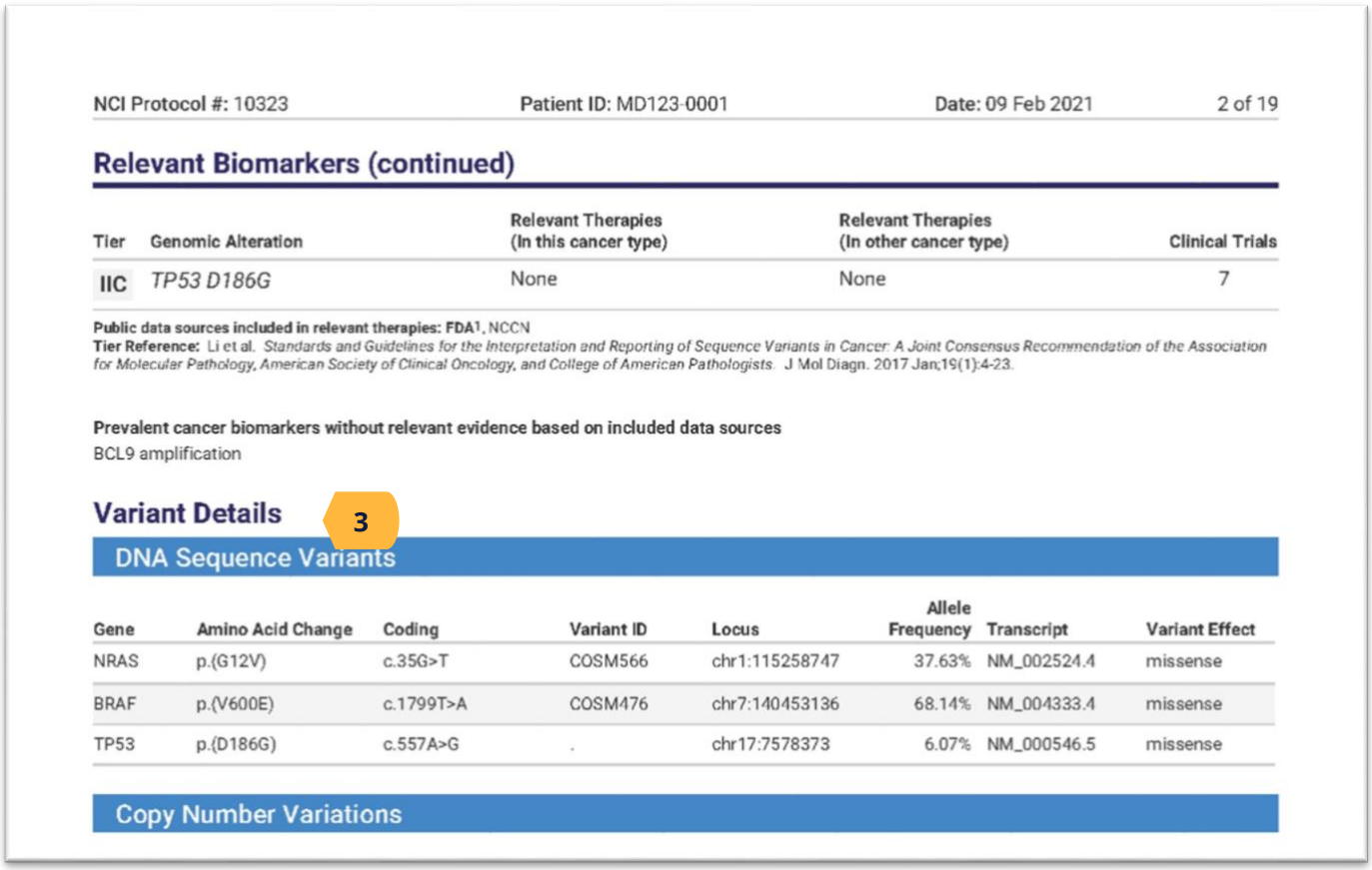
Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*BRAF V600E*	atezolizumab + cobimetinib + vemurafenib [1]	binimetinib + encorafenib [1] cetuximab + encorafenib [1]	59

1. Relevant Findings

This table lists key cancer genes tested for. If a gene tested for was found, the description and location of any gene mutations are included.

2. Relevant Biomarkers

This table lists therapies (treatments) based on the cancer type and specific biomarkers found in the tumor. The list includes therapies for a specific cancer type as well as for other types of cancers that have the same biomarkers. Different cancer types that share biomarkers may respond to the same biomarker-targeted therapies.



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Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*TP53 D186G*	None	None	7

Public data sources included in relevant therapies: FDA[1], NCCN
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

Prevalent cancer biomarkers without relevant evidence based on included data sources
BCL9 amplification

Variant Details 3

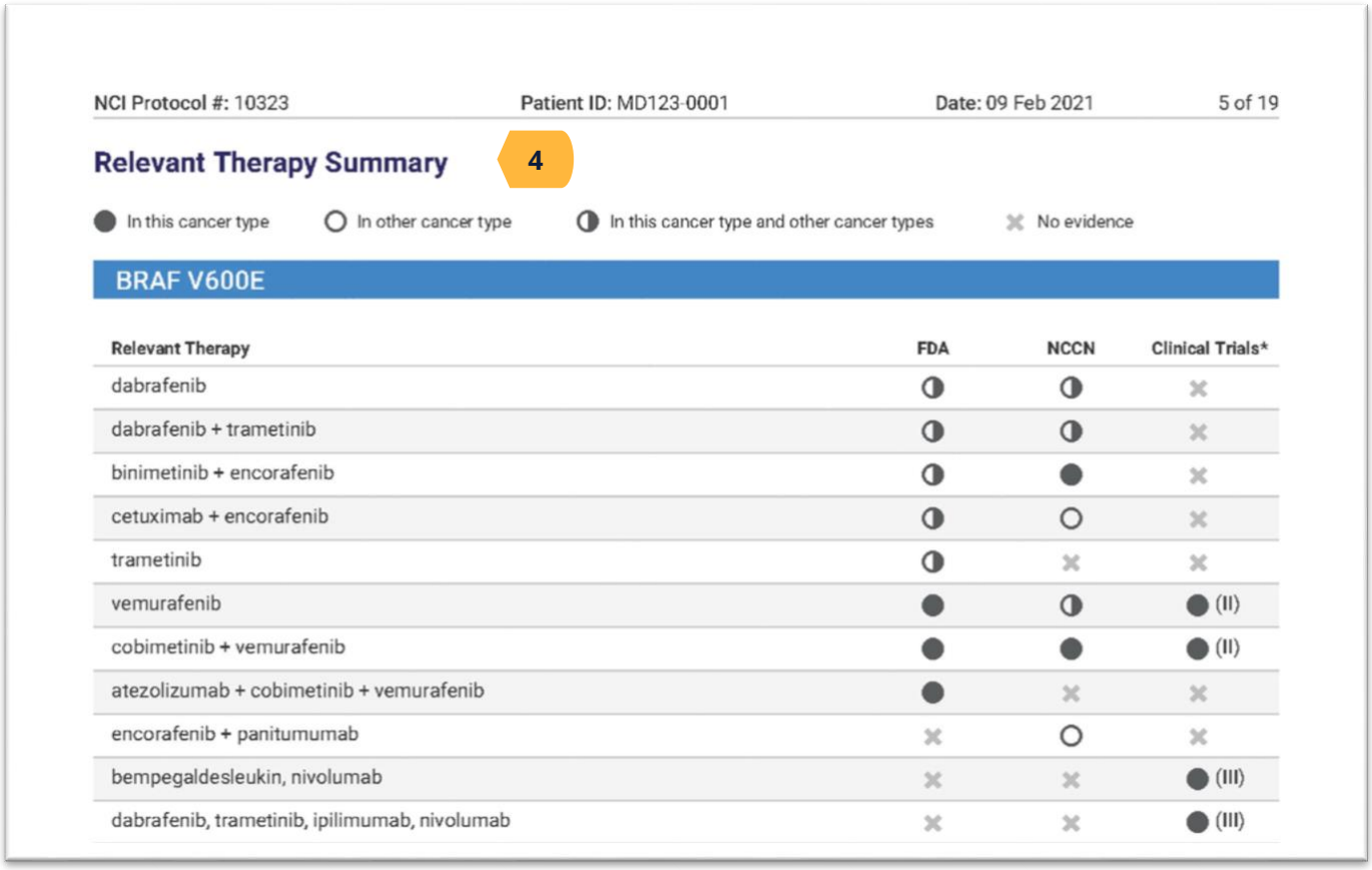
DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
NRAS	p.(G12V)	c.35G>T	COSM566	chr1:115258747	37.63%	NM_002524.4	missense
BRAF	p.(V600E)	c.1799T>A	COSM476	chr7:140453136	68.14%	NM_004333.4	missense
TP53	p.(D186G)	c.557A>G	.	chr17:7578373	6.07%	NM_000546.5	missense

Copy Number Variations

3. Variant Details

The biomarker report lists genes that are known to be related to cancer in some way. It also lists changes (variants) in those genes found in the tumor. Doctors may find this information useful when recommending treatment. There are still some changes in cancer genes that are not understood yet. They may be included in the report if they were detected, since they have been found in many cancers. This is another reason why research on these biomarkers is important.



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Relevant Therapy Summary 4

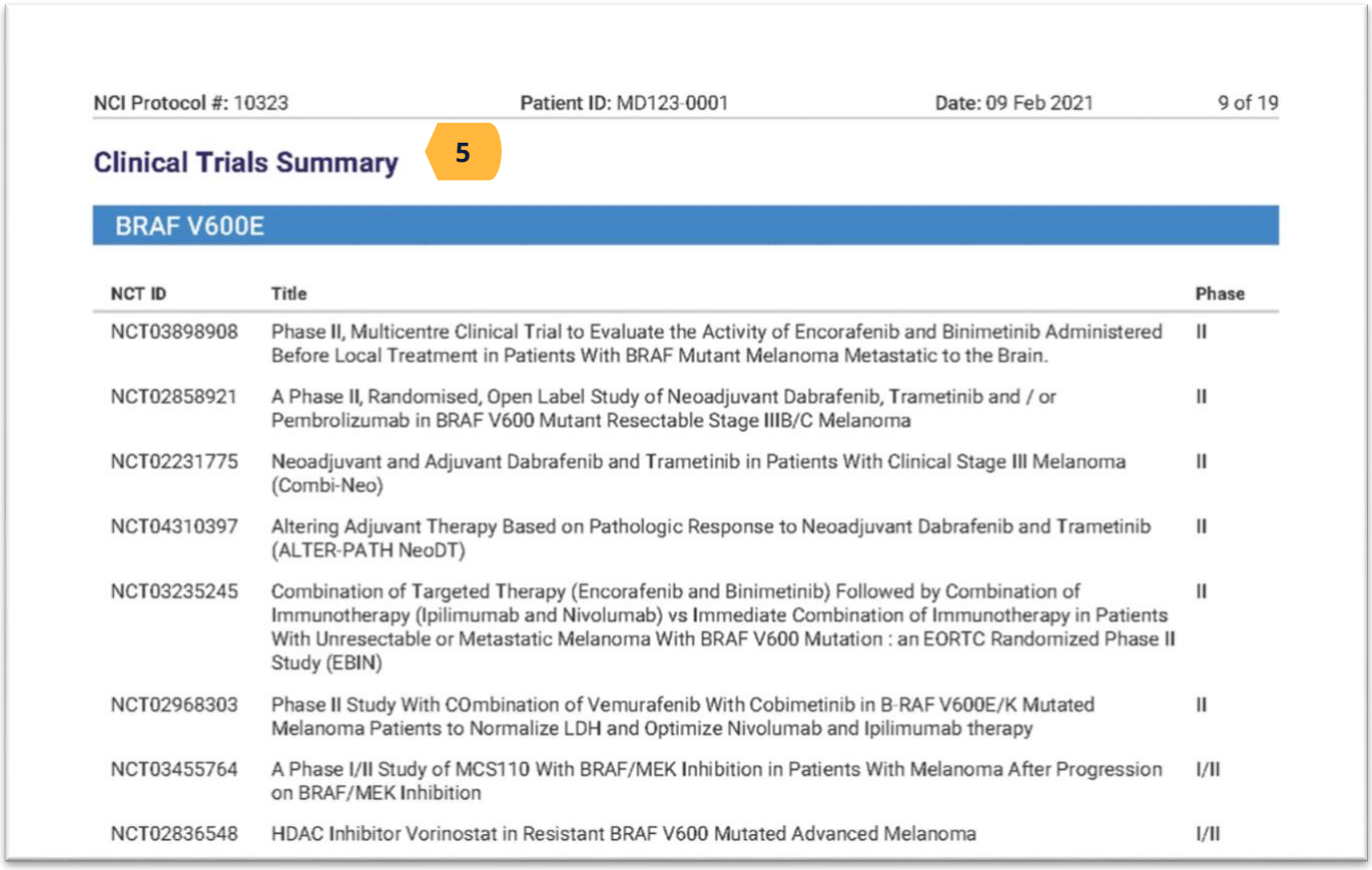
● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

BRAF V600E

Relevant Therapy	FDA	NCCN	Clinical Trials*
dabrafenib	◑	◑	✖
dabrafenib + trametinib	◑	◑	✖
binimetinib + encorafenib	◑	●	✖
cetuximab + encorafenib	◑	○	✖
trametinib	◑	✖	✖
vemurafenib	●	◑	● (II)
cobimetinib + vemurafenib	●	●	● (II)
atezolizumab + cobimetinib + vemurafenib	●	✖	✖
encorafenib + panitumumab	✖	○	✖
bempegaldesleukin, nivolumab	✖	✖	● (III)
dabrafenib, trametinib, ipilimumab, nivolumab	✖	✖	● (III)

4. Relevant Therapy Summary

The Food and Drug and Administration (FDA) and National Comprehensive Cancer Network (NCCN) publish therapy guidelines for specific cancer types. This table lists their recommended therapies based on the biomarkers found in the tumor. The table also shows whether there may be clinical trials available. A clinical trial is a type of research study that tests potential new therapies.



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Clinical Trials Summary 5

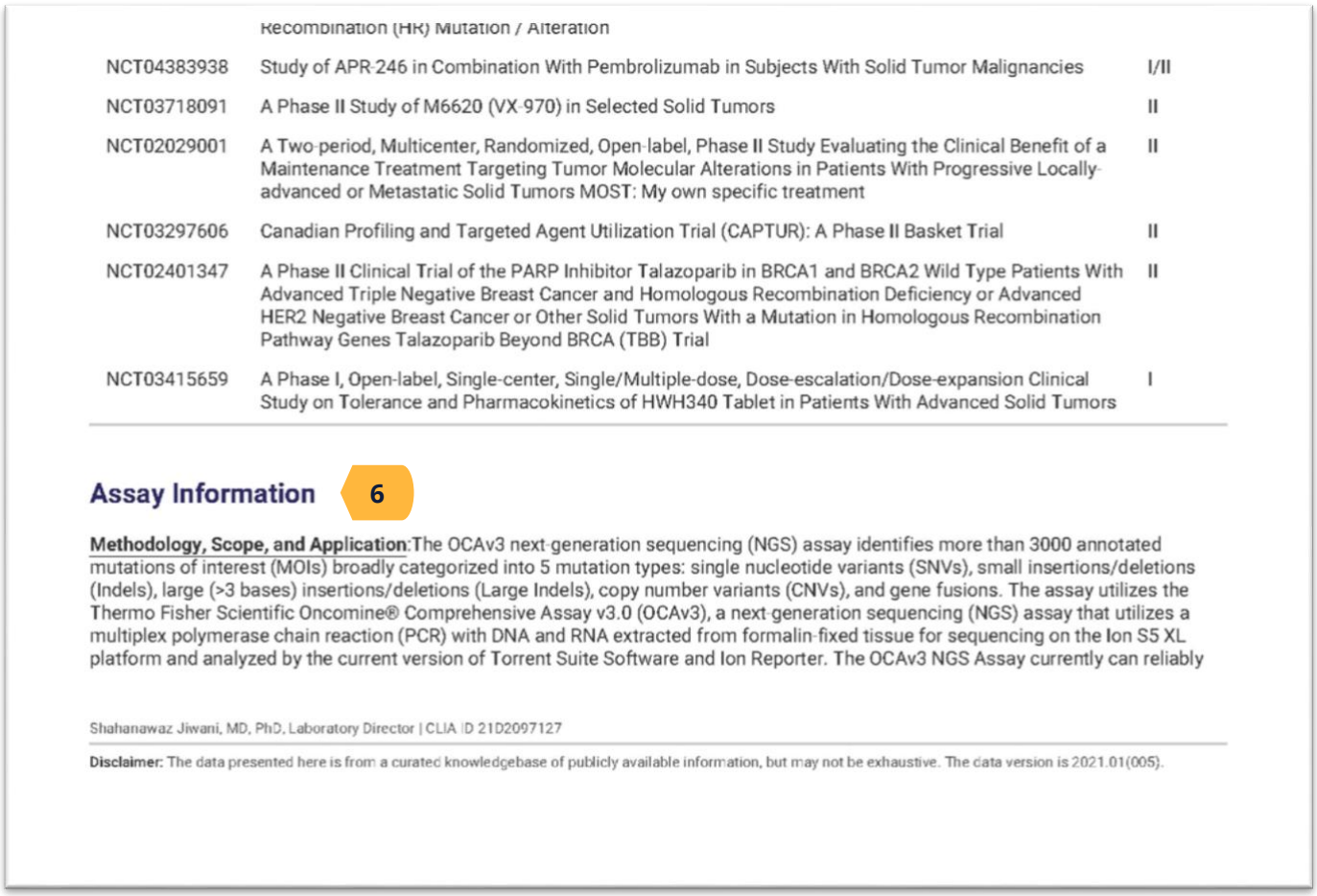
BRAF V600E

NCT ID	Title	Phase
NCT03898908	Phase II, Multicentre Clinical Trial to Evaluate the Activity of Encorafenib and Binimetinib Administered Before Local Treatment in Patients With BRAF Mutant Melanoma Metastatic to the Brain.	II
NCT02858921	A Phase II, Randomised, Open Label Study of Neoadjuvant Dabrafenib, Trametinib and / or Pembrolizumab in BRAF V600 Mutant Resectable Stage IIIB/C Melanoma	II
NCT02231775	Neoadjuvant and Adjuvant Dabrafenib and Trametinib in Patients With Clinical Stage III Melanoma (Combi-Neo)	II
NCT04310397	Altering Adjuvant Therapy Based on Pathologic Response to Neoadjuvant Dabrafenib and Trametinib (ALTER-PATH NeoDT)	II
NCT03235245	Combination of Targeted Therapy (Encorafenib and Binimetinib) Followed by Combination of Immunotherapy (Ipilimumab and Nivolumab) vs Immediate Combination of Immunotherapy in Patients With Unresectable or Metastatic Melanoma With BRAF V600 Mutation : an EORTC Randomized Phase II Study (EBIN)	II
NCT02968303	Phase II Study With COmbination of Vemurafenib With Cobimetinib in B-RAF V600E/K Mutated Melanoma Patients to Normalize LDH and Optimize Nivolumab and Ipilimumab therapy	II
NCT03455764	A Phase I/II Study of MCS110 With BRAF/MEK Inhibition in Patients With Melanoma After Progression on BRAF/MEK Inhibition	I/II
NCT02836548	HDAC Inhibitor Vorinostat in Resistant BRAF V600 Mutated Advanced Melanoma	I/II

5. Clinical Trials Summary

This table lists clinical trials that may be available for a specific type of cancer, based on gene mutations and or biomarkers found in the tumor. A clinical trial is a type of research study that tests potential new therapies.

More information on each clinical trial, such as where the clinical trial is being done, can be found at ClinicalTrials.gov.



	Recombination (HR) Mutation / Alteration	
NCT04383938	Study of APR-246 in Combination With Pembrolizumab in Subjects With Solid Tumor Malignancies	I/II
NCT03718091	A Phase II Study of M6620 (VX-970) in Selected Solid Tumors	II
NCT02029001	A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients With Progressive Locally-advanced or Metastatic Solid Tumors MOST: My own specific treatment	II
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II
NCT02401347	A Phase II Clinical Trial of the PARP Inhibitor Talazoparib in BRCA1 and BRCA2 Wild Type Patients With Advanced Triple Negative Breast Cancer and Homologous Recombination Deficiency or Advanced HER2 Negative Breast Cancer or Other Solid Tumors With a Mutation in Homologous Recombination Pathway Genes Talazoparib Beyond BRCA (TBB) Trial	II
NCT03415659	A Phase I, Open-label, Single-center, Single/Multiple-dose, Dose-escalation/Dose-expansion Clinical Study on Tolerance and Pharmacokinetics of HWH340 Tablet in Patients With Advanced Solid Tumors	I

Assay Information 6

Methodology, Scope, and Application:The OCAv3 next-generation sequencing (NGS) assay identifies more than 3000 annotated mutations of interest (MOIs) broadly categorized into 5 mutation types: single nucleotide variants (SNVs), small insertions/deletions (Indels), large (>3 bases) insertions/deletions (Large Indels), copy number variants (CNVs), and gene fusions. The assay utilizes the Thermo Fisher Scientific Oncomine® Comprehensive Assay v3.0 (OCAv3), a next-generation sequencing (NGS) assay that utilizes a multiplex polymerase chain reaction (PCR) with DNA and RNA extracted from formalin-fixed tissue for sequencing on the Ion S5 XL platform and analyzed by the current version of Torrent Suite Software and Ion Reporter. The OCAv3 NGS Assay currently can reliably

Shahanawaz Jiwani, MD, PhD, Laboratory Director | CLIA ID 21D2097127

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2021.01(005).

6. Assay Information

The biomarker test looks for three types of biomarkers:

- Single Nucleotide Variants and Indel – which are variations of a gene
- Copy Number Variants – which is the number of times a gene is repeated
- Gene fusions – when two separate genes combine together. Get more information on the genetics of cancer.