OncoPortal™ Plus

User manual

SOPHiA DDM™

Document information

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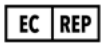
Revision history

Version	Revision name	Revision date	Summary of changes
r1	ID-60101-44-r1-EN	2022-02-23	Initial release of the document
r2	ID-60101-44-r2-EN	2022-06-24	Report attribute and section updates
r3	ID-60101-44-r3-EN	2022-08-03	Updates to somatic clinical report attributes and added example report
r4	ID-60101-44-r4-EN	2023-12-19	Updates to molecular profile sorting and filtering options. Minor updates to various sections, to reflect updated product user interface.

Document information (continued)

Symbols table

Symbol	Title
	Consult instructions for use or go to www.sophiagenetics.com
	Catalog number
	Caution
	Manufacturer
	Authorized Representative in the European Community
	Importer

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Document information (continued)

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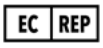

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Document information (continued)

Conventions

This document uses the following conventions:

▶ For more information...	A cross-reference to a related or more detailed topic.
[ ]	Text enclosed in square brackets indicates optional qualifiers, arguments or data.
<>	Text enclosed in angle brackets indicates mandatory arguments or data.

Document information (continued)

Intended use

SOPHiA GENETICS OncoPortal Plus is an evidence-based decision support software intended as an aid in the interpretation of variants observed in genomic next-generation sequencing data. The software annotates genomic variants in the context of published biomedical literature, professional association guidelines, publicly available databases, annotations, drug labels, and clinical trials. Based on this evaluation, the software proposes a classification and bibliographic references to aid in the interpretation of observed variants. The software is NOT intended as a primary diagnostic tool by physicians or to be used as a substitute for professional healthcare advice. Each laboratory is responsible for ensuring compliance with applicable international, national, and local clinical laboratory regulations and other specific accreditations requirements. OncoPortal Plus does not provide medical services, nor is any SOPHiA GENETICS employee engaged in the practice of medicine for or on behalf of SOPHiA GENETICS. OncoPortal Plus report content is for professional medical and scientific use only.

Contents

Contents (continued)

1 Definition of terms

A

Actionable biomarker
An actionable biomarker is linked to at least one actionable clinical association

Actionable clinical association
A reported therapeutic clinical association with guideline or FDA approval status (approval status that refer to FDA, including: FDA approved, FDA approved - Has Companion Diagnostic, FDA approved - On Companion Diagnostic, FDA contraindicated)

Analysis ID
The identifier of a single genomic analysis.

Annotation
Adding knowledge to observed variants.

B

Biomarker
A molecular feature that has clinical relevance or potential clinical relevance. A biomarker is observable and can be inferred using evidence generated in the analysis of a sample. A biomarker can be defined at the protein level, for example, BRAF V600E, or at the category level, for example, BRAF mutant. A biomarker can be related to a gene or to features at the level of multiple genes or the genome. A biomarker can also be a wild-type gene.

C

Clinical association
A clinical association is defined by published research, guidelines, or drug approvals, and links a molecular profile with a clinically relevant finding in the context of a disease.

Copy number variation
A CNV is when the number of copies of a specific gene varies between individuals.

D

Diagnostic clinical association
Clinical association with type "diagnostic (D)"

G

Gain of function
A genetic variant type in which alterated genes possess new molecular functions or patterns of expressions.

Gene
A sequence of nucleotides in DNA or RNA that is inherited and encodes the synthesis of RNA or proteins.

I

INDEL
A mutation with a blend of insertion and deletion.

L

Loss of function
A mutation that results in a decreased protein function.

M

Micro satellite instability
Occurs when the number of repeated micro satellite DNA bases is different from when the micro satellite was inherited.

Molecular profile
A combination of biomarkers that has (potential) clinical relevance.

P

Pathogenicity flag
A user annotation that labels a variant on a given pathogenicity scale.

Patient sample
A sequencing sample or reaction.

Prognostic clinical association
Clinical association with type "prognostic (P)"

1 Definition of terms (continued)

S

Single nucleotide variant
A substitution of one nucleotide for another. SNVs can be rare in one population, yet common in another population.

T

Therapy
Therapies with potential benefit in tumor are defined as Therapies linked to actionable clinical association with: 1) tier I and 2) Effect equal to "Sensitive" or "Predicted Sensitive". Therapies with potential benefit in different tumor type are defined as Therapies linked to actionable clinical association with: 1) tier II and 2) Effect equal to "Sensitive" or "Predicted Sensitive". Therapies with lack of potential benefit are defined as Therapies linked to actionable clinical association with: 1) tier I or II and 2) Effect is equal to "Resistant" or "Predicted Resistant" or "No benefit" or "Decreased response".

Tumor mutational burden
A predictive biomarker which defines the total number of mutations within the DNA of cancer cells.

U

User annotation
An annotation created by a platform user for platform concepts.

V

Variant
Genome-level biomarkers that are described as localized states of the genomic sequence.

2 Warnings and limitations of use

The limitations of OncoPortal Plus are the following:

- When assessing wild-type status, OncoPortal Plus does not take coverage into consideration. To ensure coverage is adequate to report a wild-type genes, please assess coverage warnings in SOPHiA DDM™.
- Clinical trials are curated by JAX-CKB™ according to the following criteria:
  - Trials located in the US, Canada, France, Germany, Italy, Belgium, Spain, and Austria.
  - Trials are curated for drugs that are targeted therapies or immunotherapies.
- There may be other clinical trials available.

  ▶ For more information, refer to "Clinical Trials view" on page 31.
- OncoPortal Plus is only available for analyses that are run after OncoPortal Plus has been activated on your account. When accessing analyses prior to the date of OncoPortal Plus activation, OncoPortal Plus data will not be available.

3 Data processing

Data hosted in OncoPortal Plus is processed under the conditions defined in the SOPHiA GENETICS General Terms and Conditions.

For information on data processing operations, please contact the SOPHiA GENETICS Data Protection Office (privacy@sophiagenetics.com).

4 Storage and handling

There are no storage and handling requirements for OncoPortal Plus.

5 Components and setup

No additional setup is required for OncoPortal Plus.

6 About OncoPortal Plus

OncoPortal Plus is a web-based application that presents published clinical and pre-clinical research, guidelines, and drug approvals from a central knowledgebase and allows you to filter, browse, and select relevant information to add to the final report.

OncoPortal Plus is a module of SOPHiA DDM, and can be accessed from an interpretation project within SOPHiA DDM.

SOPHiA DDM is a cloud-based Software-as-a-Service platform for data-driven medicine.

6.1 Genetic analysis workflow

A typical genetic analysis Next Generation Sequencing (NGS) workflow consists of the following steps, refer to Figure 1:

1. Genetic sequencing of the samples, and upload of the sequencing files on the SOPHiA DDM platform.
2. Alignment and variant calling.
3. Variant annotation based on evidence from databases, published clinical studies and guidelines
4. Variant interpretation using SOPHiA DDM interpretation tools (filtering, variant flagging, and classification).
5. Clinical interpretation and selection of clinical evidence for report in OncoPortal Plus.
6. Report generation.

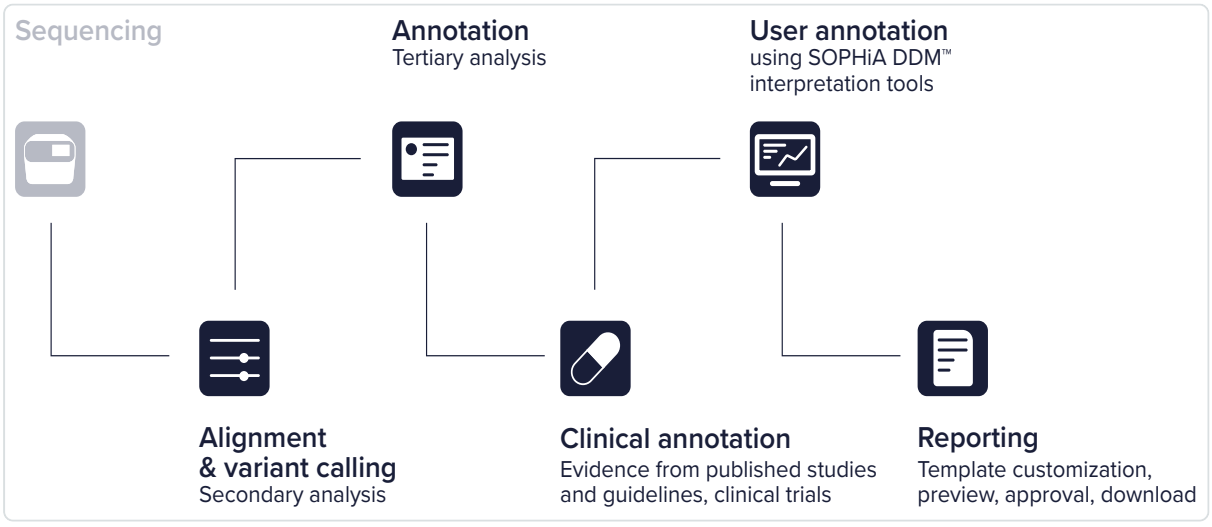


Figure 1: NGS variant detection, annotation and reporting workflow

SOPHiA GENETICS offers custom template creation. For more information, refer to the Report Generator User manual.

7 Installation

There are no installation requirements for OncoPortal Plus.

- For information on how to access OncoPortal Plus, refer to "Access OncoPortal Plus" on page 17.

7.1 Software requirements

For optimized performance of the OncoPortal Plus, your software configuration should match the requirements listed in this section.

7.1.1 Web browser requirements

OncoPortal Plus is optimized for Google Chrome™ web browser version 100 and MS Edge version 99.

7.2 Hardware requirements

OncoPortal Plus was developed to support 1280 x 800 px as a minimum display size. For optimal performance, we recommend using a standard HD screen 1920 x 1080 px.

8 Secured access

OncoPortal Plus provides secured access, to ensure the security of your SOPHiA GENETICS applications and data.

8.1 Access OncoPortal Plus

Access to OncoPortal Plus is via SOPHiA DDM.

Ask your SOPHiA GENETICS representative or contact support to request activation of OncoPortal Plus on your account.

Once active, access OncoPortal Plus by selecting the ***OncoPortal*** tab within an interpretation project in SOPHiA DDM.

8.2 Sign in

SOPHiA DDM automatically signs you in to OncoPortal Plus.

When you sign in, the onboarding window opens.

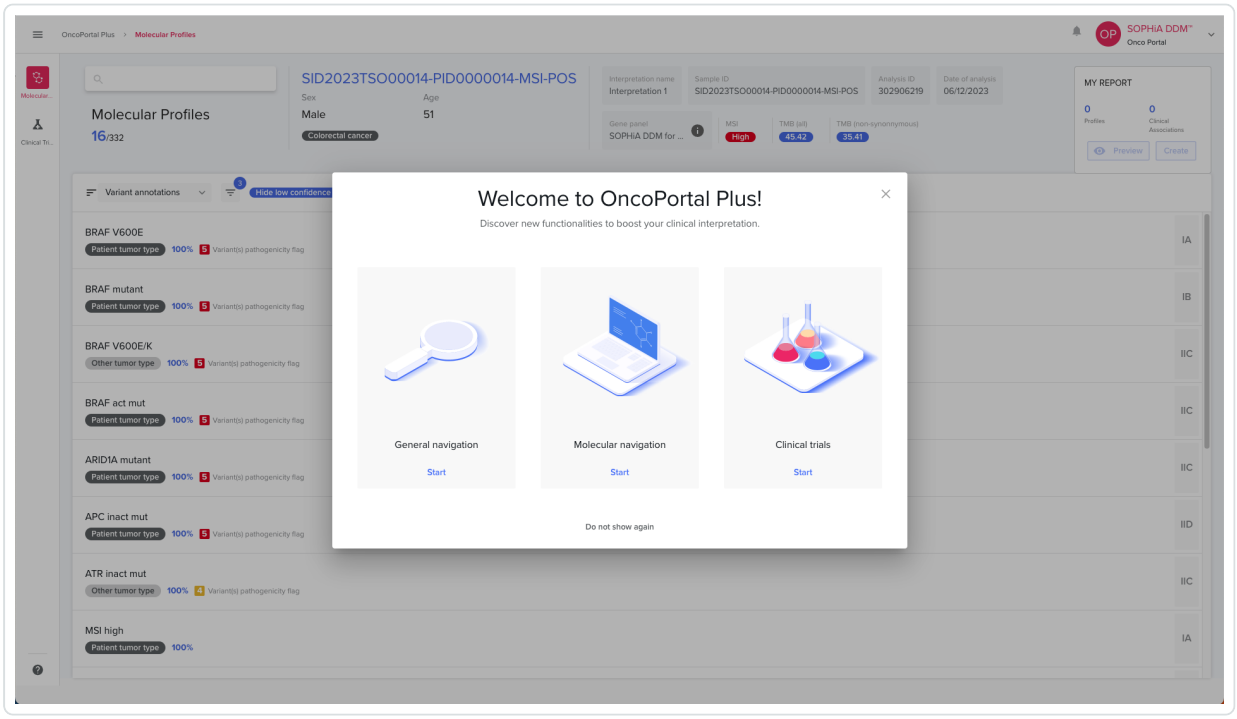


Figure 2: OncoPortal Plus in-app onboarding window

To skip onboarding after your next sign in, select ***Do not show again***.

The onboarding feature is always available in the Help menu.

8 Secured access (continued)

8.3 Sign out

To sign out from OncoPortal Plus:

1. From any OncoPortal Plus view, select your user avatar.

   The user information panel opens.

2. Select ***Sign out***.

   A confirmation window opens.

3. Select ***Sign out***.

9 SOPHiA DDM Overview

SOPHiA DDM comprises several modules that operate as separate web applications and offer additional annotation and interpretation tools/features and final report generation, including:

- OncoPortal Plus
  - ▶ For more information, refer to "About OncoPortal Plus" on page 15.
- Report Generator
  - ▶ For more information, refer to "Reporting overview" on page 36.

OncoPortal Plus is a specialized tool that allows you to view and filter evidence from a clinical knowledgebase, based on molecular profiles and genetic variations detected using SOPHiA DDM.

The Report Generator module allows you to create, preview, select a template to be applied, download, print a report, and transition the report's status by approving or rejecting a report.

Somatic gene variant annotations and related content are powered by, without limitation, The Jackson Laboratory Clinical Knowledgebase (JAX-CKB).

For more information on the use of the native SOPHiA DDM application and analysis overview, refer to the SOPHiA DDM Operation manual.

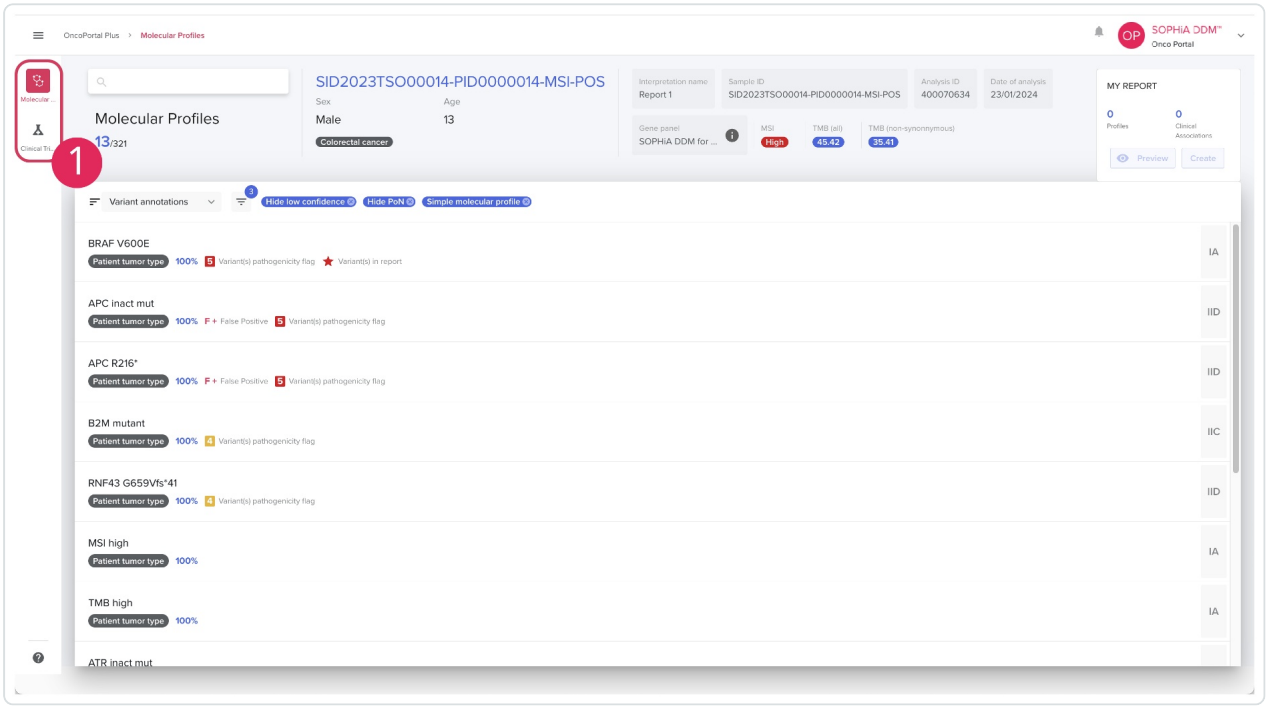
This document focuses on the usage of OncoPortal Plus and the Report Generator web applications. SOPHiA DDM is referred to only as part of the workflow.

10 OncoPortal Plus views

OncoPortal Plus consists of the following views:

- *Molecular Profiles*
- *Clinical Trials*

The views are accessed from the navigation bar.



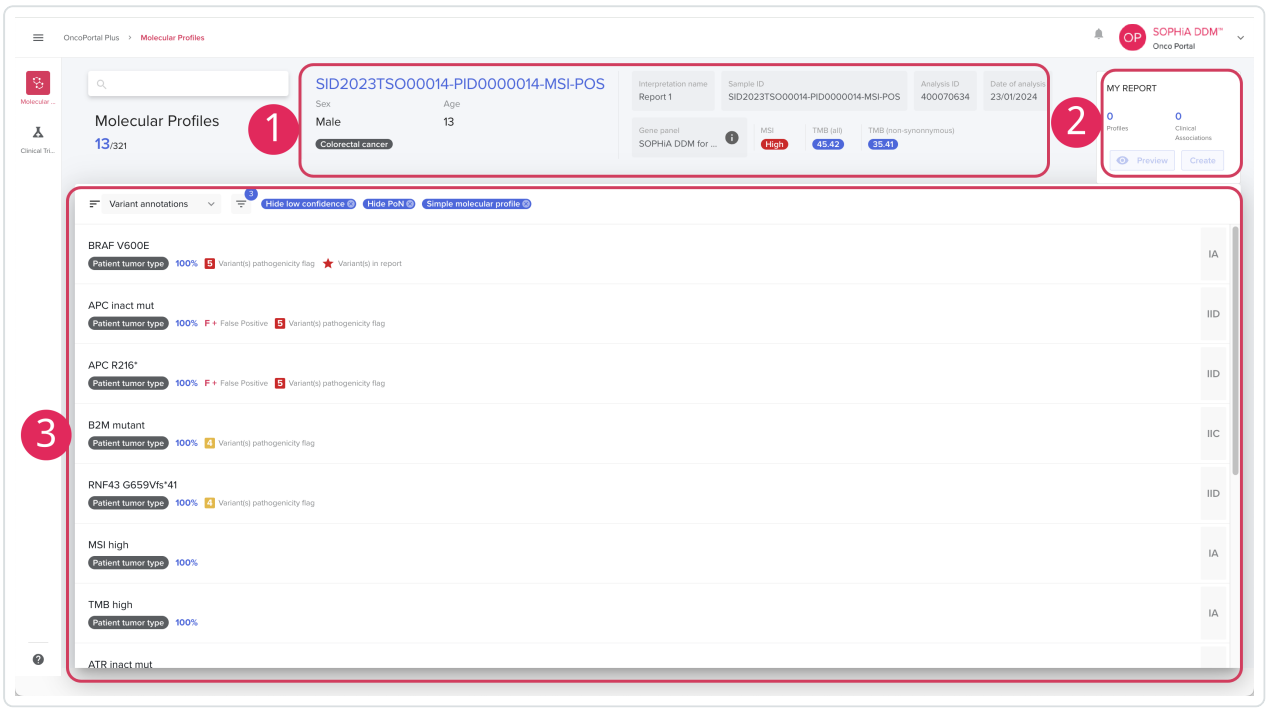
Number	Description	Details
1	Navigation bar	Allows you to switch between the ***Molecular Profile***s view and the ***Clinical Trials*** view.

Figure 3: OncoPortal Plus landing page

10 OncoPortal Plus views (continued)

10.1 Molecular Profiles view

When you enter the application, the ***Molecular Profiles*** view is shown.



Number	Description	Details
1	Project data	Provides static metadata related to the patient sample, analysis, and project. For more information, refer to "Project data" on page 22.
2	MY REPORT	Provides a summary of the information the user has added to the OncoPortal Plus report. For more information, refer to "MY REPORT" on page 22.
3	Molecular profile information	Provides more details about the molecular profile. Tumorigenesis is enabled by genome instability. As such, cancers contain combinations of mutations, and it is important to consider the overall molecular profile of the tumor in addition to assessing mutations in isolation. OncoPortal Plus provides clinical annotations based on relevant molecular profiles that are detected, or partially detected, in the sample. A molecular profile can comprise one or more biomarkers, and this allows users to see and report important biomarker interactions. For more information, refer to "Molecular Profiles" on page 23.

Figure 4: Molecular Profiles view

A combination of molecular features can be clinically relevant, for example, confer resistance to therapies.

JAX-CKB is the data source for OncoPortal Plus biomarkers, molecular profiles, clinical trials, and clinical associations. Select the OncoPortal Plus icon, in the top-right corner of the screen, to access information about the database version.

10 OncoPortal Plus views (continued)

10.1.1 Project data

This section contains the following static metadata related to the patient sample, analysis, and project:

- ***Interpretation name***: The name of the interpretation project created in SOPHiA DDM
- ***Patient ID***
- ***Patient info***: Patient calculated age and sex
- ***Disease***: The disease term entered for the patient in SOPHiA DDM
- ***Sample ID***: The sample reference as entered in SOPHiA DDM
- ***Run reference***: The run request reference as entered in SOPHiA DDM
- ***Analysis ID***: The SOPHiA DDM analysis ID
- ***Date of analysis***
- ***Gene panel***: The gene panel used for analysis
- ***Interpretation scope***
- ***Root gene panel***
- ***Tumor cell %***: As entered in the ***Interpretation Project Specimen Information*** tab in SOPHiA DDM
- ***MSI***: Micro Satellite Instability (MSI) status analysis results
- ***TMB (all)*** and ***TMB (non-synonymous)***: Tumor Mutational Burden (TMB) scores

MSI and TMB scores (all and non-synonymous) are only available for some applications. Please consult the operation manual for the specific application for more details.

Patient information is an extension of the SOPHiA DDM interpretation. Patient information is imported from SOPHiA DDM.

10.1.2 MY REPORT

This section provides a summary of what has been reported in OncoPortal Plus. To preview a report, you must return to SOPHiA DDM.

When you select ***Create report***, you will be advised to return to SOPHiA DDM to begin the reporting workflow. For more information, refer to "Generate a report" on page 40.

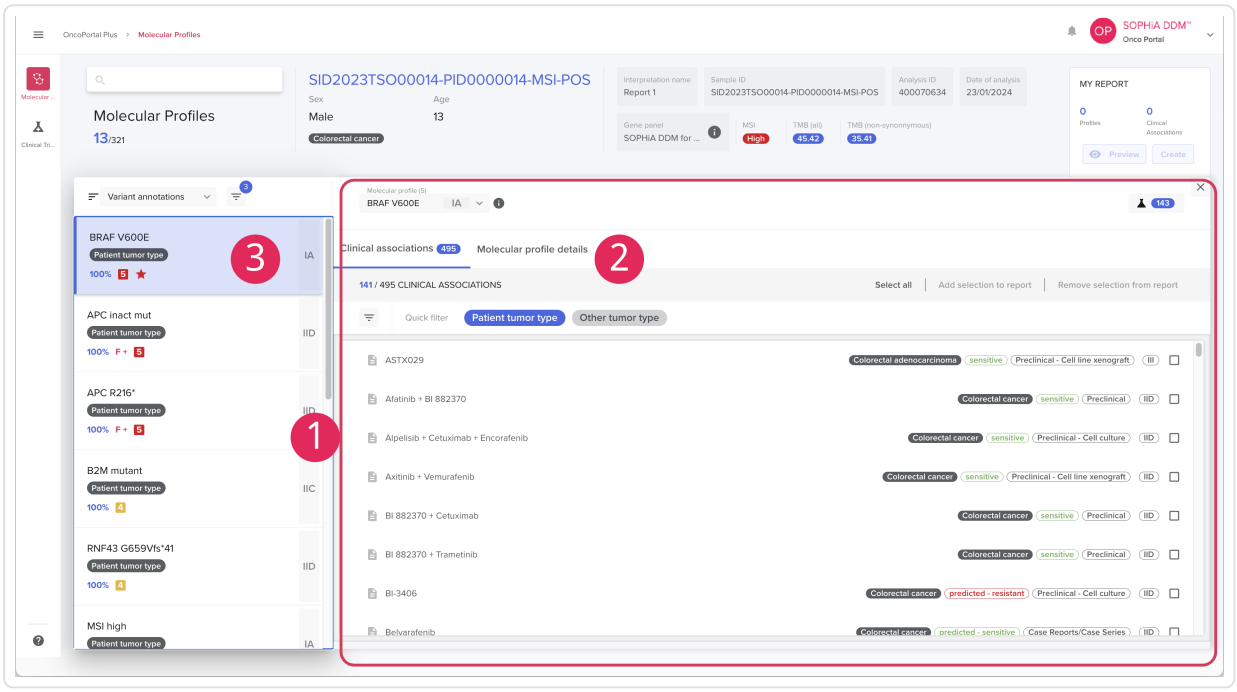
10 OncoPortal Plus views (continued)

10.1.3 Molecular Profiles

You can click on a molecular profile to view more information. Refer to Figure 5.

To switch between the default clinical association view and the molecular profile details, select the ***Molecular profile details*** tab.

To go back to the clinical associations view, select the ***Clinical associations*** tab.



Number	Description	Details
1	Molecular profile information	The default clinical association view of a molecular profile.
2	Molecular profile details tab	Allows you to switch between the default clinical association view and the molecular profile details.
3	Molecular profile group	Related molecular profiles, for example BRAF V600E, V600X, inact mut, mutant, are grouped into one molecular profile card in the left menu. Only simple molecular profiles are grouped. Complex molecular profiles with multiple biomarkers are listed separately. In a group the molecular profile with the highest clinical significance (tier) is displayed by default. If there are multiple molecular profiles with the highest tier, the profile that is most closely related to the variant is selected. All other molecular profiles, and related clinical associations, can be selected from the drop-down.

Figure 5: Molecular profile information

10 OncoPortal Plus views (continued)

The molecular profile details shown are the following:

- Molecular profile name
- Information button

  When you click the information button, a popup provides a description of the gene and the biomarker(s) for each component of the molecular profile.
- Biomarker tabs

  Separate tabs provide additional information on each biomarker.

  Biomarkers can have three possible statuses: detected, not tested, and undetermined. Biomarkers are labeled as undetermined when, for example, a gene has an undetermined copy number, or for a TMB status that is not determined by the system.

  For each biomarker, OncoPortal Plus displays the supporting variant(s) or other molecular feature detected in SOPHiA DDM. Select any variant to display *VARIANT OVERVIEW* and view the following information:

  - *PATH FROM DETECTED VARIANT* shows the decision path used by the system to link a variant to a biomarker. OncoPortal Plus gives users a level of confidence between the variant and the biomarker, with 100% meaning high confidence that the variant has that biomarker as a consequence. A low score means that the link between the variant and the biomarker may not be true.
  - Wild-type class.

    ▶ For more information, refer to "Wild-type genes" on page 35.

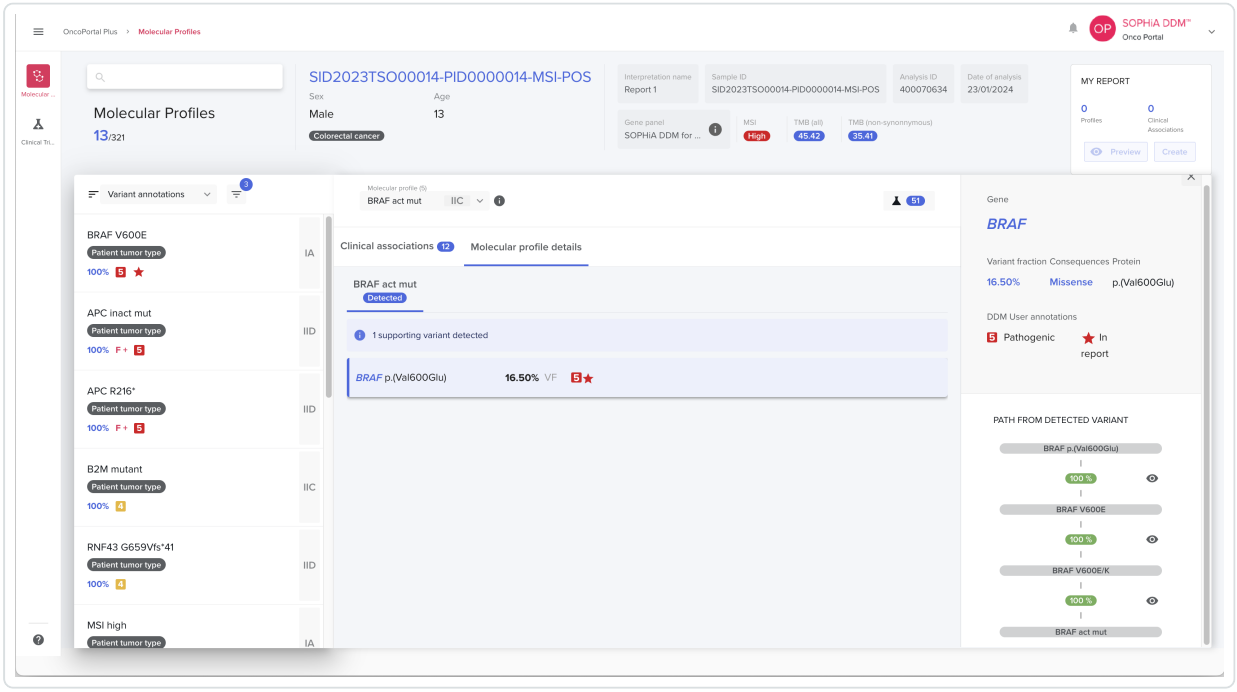


Figure 6: Molecular profile details

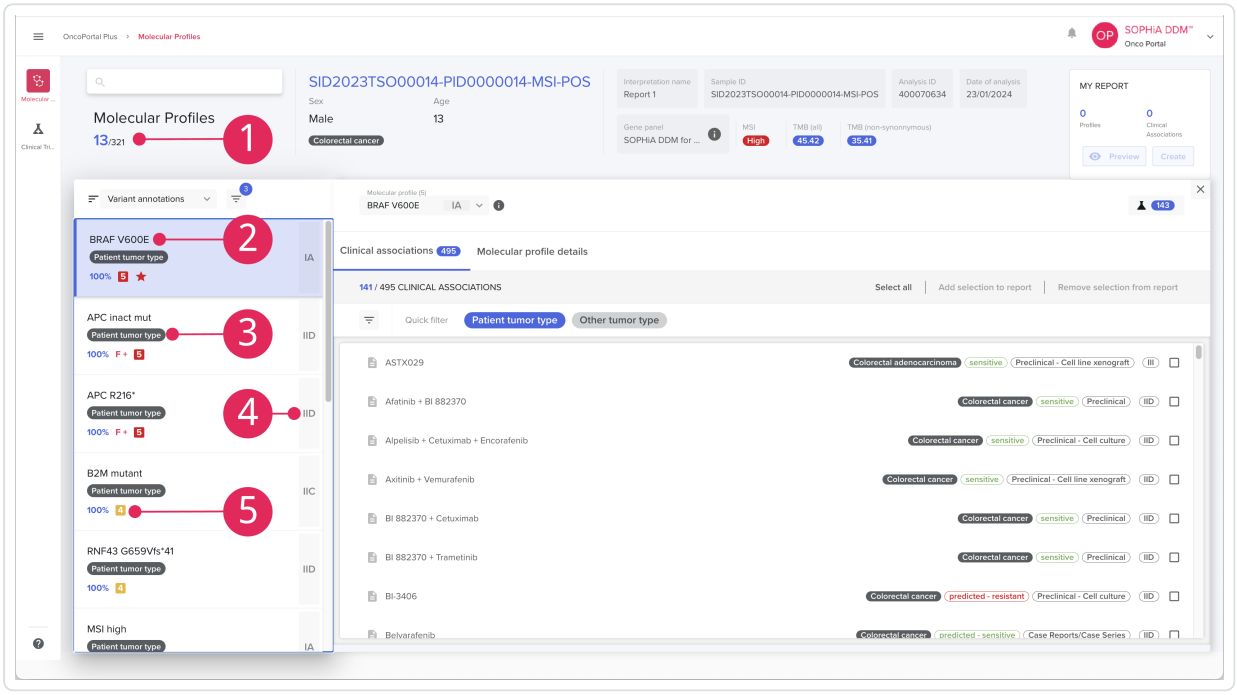
For more information on variant types, refer to the SOPHiA DDM Operation manual.

10 OncoPortal Plus views (continued)

Molecular Profiles list

The ***Molecular profiles*** tab displays a pre-filtered list of molecular profiles related to the sample.

▶ For more information, refer to "Sort and filter molecular profiles" on page 39.



Number	Description	Details
1	Counter	Contains the number of available molecular profiles based on the filters applied, over the total number of molecular profiles detected in the patient sample.
2	Molecular profile name	The molecular profile name can be simple, for example, EGFR exon19 del, where only one biomarker composes the molecular profile. Molecular profiles can comprise several biomarkers, each separated by **+** as follows: • EGFR exon19 del + MET pos • ALK Fus. + EGFR exon19del + EGFR T790M
3	Tumor type indicator	Indicates whether there are clinical associations for the patient's tumor type or other tumor types.
4	Tier	Clinical significance. The tier and evidence level according to the AMP/ASCO/CAP guidelines. For more information, refer to "Tier classification" on page 30.
5	Indicators	Contains additional variant manual annotations and other variant level information. For more information, refer to "Indicators" on page 26.

Figure 7: Molecular profiles tab

10 OncoPortal Plus views (continued)

Indicators

The first indicator is the 'Sample overlap'. It represents the fraction of the molecular profile that was actually detected in the sample.

► For more information, refer to "What is a molecular profile?" on page 32.

Manual annotations:

This set of indicators shows if a user has added manual annotations, in SOPHiA DDM, to any variant supporting the given molecular profile. Within SOPHiA DDM you can add the following manual annotation types:

- Pathogenicity level of variants, represented as numbers 1 to 5.
- Variants that have been added to the report in the interpretation project.
- False positive variants.

Other indicators:

- Low confidence indicator Low confidence which labels any variant that is not retained by the bioinformatic pipeline.
- Panel of Normals (PoN) indicator.

Comments added in SOPHiA DDM are not displayed in OncoPortal Plus.

10 OncoPortal Plus views (continued)

Quick filters

Quick filters allow you to switch between lists of clinical associations without entering the filter settings.

You can filter molecular profiles by using the following quick filters, both of which are selected by default:

Parameter	Description
Patient tumor type	Filter for clinical associations linked to the patient's tumor type.
Other tumor type	Filter for clinical associations linked to other tumor types.

Table 1 Quick filters

10 OncoPortal Plus views (continued)

Molecular profile filters

You can filter molecular profiles by the following parameters:

Parameter	Description
Disease	Filter for one or more diseases, including the patient's diseases. For more information, refer to "Project data" on page 22.
Tier	Filter by AMP/ASCO/CAP tier (clinical significance). For more information, refer to "Tier classification" on page 30.
Association type	Filter based on the type of clinical association, for example, therapy, diagnosis, prognosis, emerging evidence, or risk factor.
Approval authority	Filter therapies by approval authority, for example, FDA.
Response type	Filter by the effect that a therapy has on a disease, for example, the disease is sensitive, or has a resistance to a therapy, or the therapy has no effect on the disease.
TMB biomarkers	Filter for TMB biomarkers, TMB high or TMB low, to focus on relevant clinical associations based on your assessment of the TMB status of the sample.  TMB status is not predicted by SOPHiA DDM. You must review the TMB scores to assess, based on your knowledge, if the sample should be considered TMB high or low.
Sample overlap	Filter by the extent of overlap of biomarkers that a molecular profile has with the analyzed sample. Set the filter to 100% if you only want to see molecular profiles where all biomarkers have been detected in the sample.
Variant annotation	Filter molecular profiles based on manual variant annotations added in SOPHiA DDM, by pathogenicity level (1–5) or reported variants.
Low confidence	Filter out molecular profiles that are supported only by low confidence variant calls. If a molecular profile is linked to variants that are both retained and low confidence, the molecular profile remains in the list and the low confidence variants are still visible.  Low Confidence variant is not to be confused with the confidence of a link between a variant and biomarker.
Panel of Normals	If a matched normal is not available, filter out molecular profiles that are linked only to variants with a >1% frequency in healthy populations, and can be considered germline polymorphisms. The frequencies are reviewed in the following databases: GnomAD, 1000 Genomes Project, and ExAC. The versions used are displayed in the interpretation project view in SOPHiA DDM.
Molecular Profile type	Filter by the type of molecular profile, for example, Simple Molecular Profiles, Complex Molecular Profiles, or Wild-type genes.

Table 2 Molecular profile filtering parameters

10 OncoPortal Plus views (continued)

Molecular profile sorting options

You can sort molecular profiles by the following parameters:

Parameter	Description
Variant annotations	Sort molecular profiles based on user annotations on the linked variants. Molecular profiles are sorted according to the following priority of user annotations: • In Report • Pathogenicity 5>4>3>null>2>1
Variant fraction (%)	Sort molecular profiles based on variant abundance in the sample, in descending order.
Sample overlap (%)	Sort molecular profiles by the number of biomarkers detected in the molecular profile, as a percentage of the total number of biomarkers.
Clinical significance	Sort molecular profiles by clinical significance according to the following priority: • On AMP/ASCO/CAP tier. For more information, refer to "Tier classification" on page 30.
Rank	Sort molecular profiles by relevance to the sample, considering: • Relevance, based on the confidence of the link from the molecular profile to the sample. • Clinical significance. • Sample overlap. • Number of biomarkers in the profile.

Table 3 Molecular profile sorting parameters

Clinical associations

A list of the clinical associations for the molecular profile is given on this panel. This displays the number of clinical associations linked to the selected molecular profile, and how many clinical associations have been filtered.

The filters applied to the molecular profiles are propagated to related clinical associations. A second filtering option is available at the top of the clinical association list. This allows you to quickly overwrite the primary filtering settings and to expand or restrict the given list of clinical associations.

The filtering option only affects the list of clinical associations in a given molecular profile panel and is not propagated to the other molecular profiles.

For each clinical association, the following information is shown:

- Related disease
- Tier
  - ▶ For more information, refer to "Tier classification" on page 30.
- Approval authority (for therapies)
- Response type (for therapies)
- Therapy name (for therapies)
- Diagnosis, Prognosis, or Emerging Evidence, in the case of clinical associations that are no related to therapies

10 OncoPortal Plus views (continued)

Click on a clinical association to display a details panel providing more information, including summary and supporting evidence.

For more information on adding clinical associations to a report, refer to "Add clinical associations to a report" on page 39.

Tier classification

The AMP/ASCO/CAP tier and evidence level criteria are provided in " AMP/ASCO/CAP classification guide" on page 30.

Tier	Clinical significance	Description	Details
IA	Strong	Biomarker predicts response or resistance to an FDA approved therapy, according to drug label or professional guidelines for this diagnosis. Biomarker included in professional guidelines is prognostic or diagnostic for this diagnosis.	Tier and evidence level provided by JAX-CKB.
IB	Strong	Biomarker predicts response or resistance to a therapy for this diagnosis based on well powered studies.	Tier and evidence level for therapies provided by JAX-CKB.
IIC	Potential	Biomarker is associated with response or resistance to an FDA approved therapy, according to drug label or professional guidelines, but only for different diagnosis. Biomarker predicts response to a therapy for a different diagnosis based on well powered studies. Biomarker is an inclusion criterion for an active clinical trial. Biomarker is prognostic or diagnostic based on clinical studies.	Tier IA and IB evidence in JAX-CKB for a tumor type different to the patient disease selected in SOPHiA DDM.
IID	Potential	Biomarker shows plausible response or resistance based on case or preclinical studies.	Tier and evidence level for therapies provided by JAX-CKB.
III	Unknown	Biomarker has uncertain clinical significance and not known to be likely benign, or benign.	Biomarker is not listed as benign or likely benign in ClinVar. Biomarker is present in COSMIC or present at low frequency in population databases.

Table 4 AMP/ASCO/CAP classification guide

Clinical trials

The ***Clinical trials*** label on the right side of the panel indicates the number of clinical trials associated with the given molecular profile.

Click on the ***Clinical trials*** label to access the corresponding list of clinical trials.

Clinical trials are curated by JAX-CKB(TM) according to the following criteria:

- Trials located in the US, Canada, France, Germany, Italy, Belgium, Spain, and Austria.
- Trials are curated for drugs that are targeted therapies or immunotherapies.

10 OncoPortal Plus views (continued)

10.2 Clinical Trials view

To view clinical trials select the left panel tab. Doing this shows the full list of clinical trials associated with the analysis. Clinical trials are matched to the analysis by molecular profile and gene. You can see the terms used to match the trials as indicators in the clinical trial list and in the details panel. You can sort and filter with criteria specific to clinical trials.

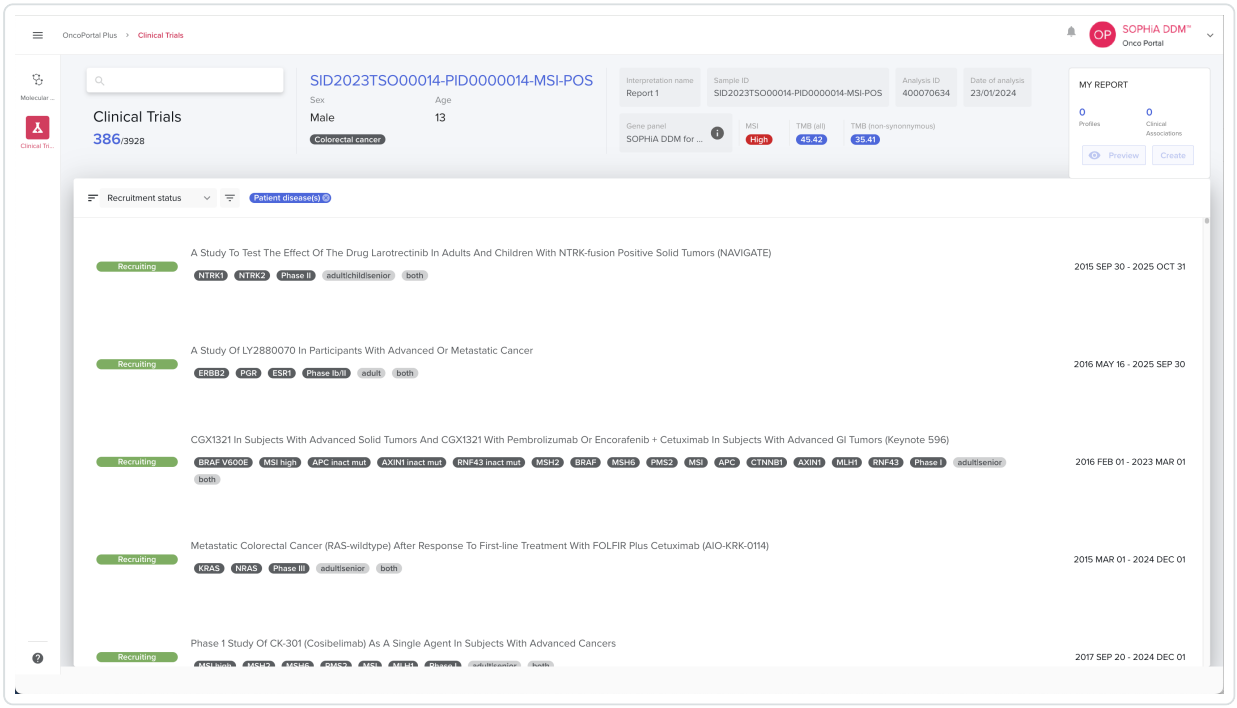


Figure 8: Clinical Trials view

11 What is a molecular profile?

A molecular profile is one or more biomarkers, as described in published studies, professional treatment guidelines, and drug approvals.

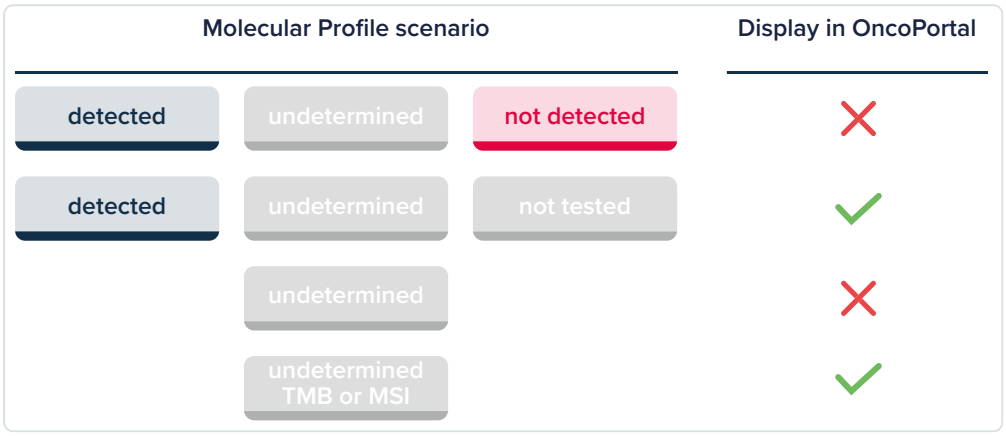


Figure 9: Molecular profile scenarios

For a molecular profile to be shown in OncoPortal Plus, the profile must:

- Contain a minimum of one detected biomarker, or undetermined TMB biomarker
- Not contain an undetected biomarker

▶ For more information on biomarkers, refer to "Biomarkers" on page 32.

▶ Molecular profile scenarios are given in Figure 9.

OncoPortal Plus lists molecular profiles rather than individual variants, because this shows relevant biomarkers and biomarker interactions while it eliminates redundant entries for biomarkers that are matched to multiple variants in the sample.

SOPHiA GENETICS OncoPortal Plus uses the JAX-CKB database as its source for all molecular profiles, biomarkers, clinical associations, and clinical trials in OncoPortal Plus.

Molecular profiles are displayed in the Molecular profiles tab.

▶ For more information, refer to "Molecular Profiles" on page 23.

11.1 Biomarkers

A biomarker is a molecular feature that has clinical relevance or potential clinical relevance, and can be a variant or wild-type gene.

▶ For more information, refer to "Wild-type genes" on page 35.

A biomarker can be defined at the molecular level, at the category level, and at the gene level. It can be related to a single gene, to features of multiple genes, or to the genome.

11 What is a molecular profile? (continued)

Biomarkers can be defined at the following levels:

- Molecular, for example, BRAF V600E
- Category, for example, BRAF activating mutant
- Gene, for example, BRAF mutant

Supported biomarkers are given in the following tables:

- SNVs/INDELs,
  - ▶ Refer to " Biomarkers related to SNVs/INDELs" on page 33.
- CNVs
  - ▶ Refer to " Biomarkers related to CNVs" on page 34.
- Fusions
  - ▶ Refer to " Biomarkers related to fusions" on page 34.
- TMB and MSI
  - ▶ Refer to " Biomarkers related to TMB and MSI" on page 35.

Biomarker type	Conditions
Molecular change, for example, G3**R, D648_Y65dup	Genomic coordinates Protein alteration, same transcript dbSNP rsid
mutant	JAX-CKB path from molecular change, or SOPHiA DDM prediction A (pathogenic, and gene is a tumor suppressor)
del exon x (deletion of exon)	SOPHiA DDM predicts a coding consequence splice
exon x del (deletion in exon)	SOPHiA DDM predicts a deletion in exon
exon x (mutation in exon)	Any variant in exon with a minimum of one match to another variant in JAX-CKB
exon x del / exon x ins	SOPHiA DDM predicts deletion or insertion in exon
inact mut (inactivating mutation)	A minimum of one match to another variant in JAX-CKB with LOF, or SOPHiA DDM prediction A (pathogenic), and gene is a tumor suppressor and not overlapped to GOF
act mut (activation mutation)	A minimum of one match to another variant in JAX-CKB with GOF, and gene is oncogene

Table 5 Biomarkers related to SNVs/INDELs

11 What is a molecular profile? (continued)

Biomarker type	Conditions
amp (amplification)	Duplication of a minimum of 80% of the gene
loh (loss of heterozygosity)	Deletion with copy number 1 of a minimum of 80% of the gene, and the chromosome is autosomal
del (deletion)	Deletion with copy number 0 of a minimum of 80% of the gene
loss	Deletion with copy number 0 of a minimum of 80% of the gene
over exp (over expression)	Duplication of a minimum of 80% of the gene
exon x del / exon x ins	SOPHiA DDM predicts deletion or insertion in exon
inact mut	Match to amp, del, or loss with effect LOF
act mut	Amplification in an oncogene
mutant	If matched to act mut or inact mut
rearrange	Amplification in an oncogene

Table 6 Biomarkers related to CNVs

Biomarker type	Detected variant	Conditions
GeneA - GeneB	Gene fusion	Gene matches
GeneA fusion	Gene fusion	Matched to 5' or 3' gene
del exonX	Exon skipping	Deletion of exon x(exon only)
GeneA G54_R78del	Exon skipping	Skipped exons match
GeneA V30_R297delinsG	Exon skipping	Skipped exons match
inact mut (inactivating mutation)	Gene fusion or exon skipping	Match to LOF variant in JAX-CKB
act mut (activating mutation)	Gene fusion or exon skipping	Matched to GOF variant in JAX-CKB
mutant	Gene fusion or exon skipping	If matched to act or inact mut
rearrange	Gene fusion or exon skipping	If matched to act or inact mut

Table 7 Biomarkers related to fusions

11 What is a molecular profile? (continued)

Biomarker type	Detected feature	Conditions
MSI high	MSI status	Biomarker status is assessed for applications that output an MSI status. For applications that output MSI results in the MSI report only, the biomarker status will be undetermined
MSI negative	MSI status	For pipelines that output MSI status. If not, MSI biomarkers are set to status undetermined
TMB high	TMB score	TMB biomarkers are displayed for all samples in which TMB is analyzed, independent of the TMB scores
TMB low	TMB score	TMB biomarkers are displayed for all samples in which TMB is analyzed, independent of score

Table 8 Biomarkers related to TMB and MSI

TMB status is not predicted by SOPHiA DDM. You must review the TMB scores to assess, based on your knowledge, if the sample should be considered TMB high or low.

Biomarker MSI low cannot be assessed using the SOPHiA DDM MSI module.

11.1.1 Wild-type genes

A gene is considered wild-type if no oncogenic or clinically relevant variants are detected in the scope of the analysis. Wild-type classes defined by the system are as follows:

- Class 1:
  - The gene is included in the gene panel, and
  - no oncogenic variants are detected, and
  - no other clinically relevant variants are detected, and
  - no variants of uncertain oncogenicity are detected
- Class 2:
  - The gene is included in the gene panel, and
  - no oncogenic variants are detected, and
  - a minimum of one clinically relevant variant, or variant of uncertain oncogenicity, is detected

A variant is called clinically relevant if it has at least one clinical association in JAX-CKB.

Oncogenicity is uncertain for any variant that does not belong to the oncogenic, clinically relevant, or not clinically relevant classes.

Coverage is not taken into consideration in wild-type evaluation. You must assess coverage.

For more information on wild-type genes, refer to "Molecular Profiles" on page 23.

12 Reporting overview

The SOPHiA DDM application offers the possibility of creating a report for the genetic analysis performed. Within an interpretation project, you can select variants to include in the report.

In addition to variants, OncoPortal Plus allows you to select clinical associations to include in the report. Clinical associations include diagnostic, prognostic, and therapeutic evidence from published research and treatment guidelines.

- For more information, refer to the SOPHiA DDM Operation manual.
- For more information on reporting clinical associations, refer to "Add clinical associations to a report" on page 39.

The Reporting Module comprises the following web applications:

- Report Generator
  - For more information, refer to the Report Generator User manual.

Reports are downloaded in PDF format from the Report Generator application.

12.1 Report content

You can generate different types of reports depending on the analysis you are performing using the Report Generator. Below you can find the description of the OncoPortal Plus report template to get an overview of all the report's section. Descriptions of other reports supported by SOPHiA DDM can be found in the Report Content section of the Report Generator User manual.

You can request a custom header and footer in your request for a custom report template. For more information, refer to the Report Generator User manual.

12.1.1 OncoPortal Plus report template

OncoPortal Plus reports can be generated to report available information on reported variants and clinical associations from OncoPortal Plus. OncoPortal Plus reports contain the sections given in Table 9.

To view an example somatic variant report with labelled sections, refer to "Appendix 1. Example somatic clinical report" on page 46.

Attributes presented in OncoPortal Plus reports depend on the type of reported variant (SNV/INDEL, CNV, intergenic, fusion).

Actionability is identified if at least one actionable clinical association is added to the report.

An actionable biomarker is a predictive biomarker for FDA approved therapies or treatment guidelines.

12 Reporting overview (continued)

Section	Contents
Header	Report title Report date Logo
Footer	Report date Patient first and last name Date of birth Gender Patient and sample identifiers Page number(s)
Patient data	Patient first and last name Date of birth Gender Patient identifiers Pathology
Specimen data (Admin information section)	Specimen ID Specimen type and preservation method DNA, RNA, or NA quantity Date of specimen collection Date of specimen reception
Order data (Admin information section)	Contact details of the person who ordered the test Contact details of the person, or institution, who selected the specimen
Conclusion	User-entered free text conclusion on SOPHiA DDM
Clinical overview	Result statement: "Actionability Identified" if there are >1 Actionable biomarkers in the report, else "No Actionability Identified" Tumor cell % MSI status and TMB scores (if applicable) Count of actionable biomarkers and reported therapies
Clinical question	SOPHiA GENETICS application name Test performed (user-entered free text on SOPHiA DDM) Referral reason (user-entered free text on SOPHiA DDM)
Clinical Actionable biomarkers table	Summary table containing all reported Molecular Profiles from OncoPortal Plus and associated therapies: Therapies with potential benefit in tumor, Therapies with potential benefit in different tumortype, Therapies with lack of potential benefit
Clinical biomarkers overview	Count of reported prognostic and diagnostic biomarkers, and biomarkers with potential clinical significance
Reported variants *	Gene alteration Database annotations User annotations
Reported therapies †	Therapy name Approval status Reported molecular profiles Disease Response type References
Interpretation §	Clinical association details Gene alteration Biomarker description(s) Database and user annotation(s) (if available)

12 Reporting overview (continued)

Section	Contents
SOPHiA GENETICS methodology (Methodology section)	SOPHiA GENETICS application name SOPHiA DDM version number Pipeline ID/Revision number/Splitting ID Reference genome Sequencer name Run name and run date Analysis ID Sample ID JAX-CKB version number OncoPortal Plus version number
Lab methodology (Methodology section)	Details of lab methods for the test performed (user-entered free text on SOPHiA DDM)
Analyzed by	Username of the user who performed the interpretation
Validated by	Username of the user who approved the report (if approval workflow activated) Date of report approval Blank space for signature

* One card for each reported variant
† One card for each reported therapeutic clinical association
§ One entry for each reported molecular profile

Table 9 Somatic clinical report summary

The SOPHiA DDM default OncoPortal Plus template displays a subset of somatic specific sections, and can be augmented by adding Somatic Annexes from ***DDM Project settings***.

► For more information, refer to "Project Settings" in the SOPHiA DDM Operation manual.

13 Operating instructions

This section describes the actions that can be performed in OncoPortal Plus.

13.1 Sort and filter molecular profiles

When you first access OncoPortal Plus, the following filters are applied by default:

- Low confidence variants: Hide low confidence
- Panel of normals (PoN): Hide PoN
- Molecular Profile type: Simple Molecular Profiles

▶ For more information on filters, refer to "Molecular profile filters" on page 28.

The following sorting option is also applied by default:

- Variant annotations

▶ For more information on sorting options, refer to "Molecular profile sorting options" on page 29.

To apply a filter, or modify filter settings, do as follows:

1. From the ***Molecular profiles*** tab, click the filtering icon.
2. Select the filters to be applied.
   ▶ For more information on filters, refer to "Molecular profile filters" on page 28.
3. To save the filter, click outside of the filter menu to apply the changes.
4. To use the same filter settings each time you access OncoPortal Plus, select ***Save as default***.
5. To reset the filter, select ***Reset filter***.

Alternatively, use the search field to search for specific molecular profile(s).

When searching for a molecular profile, use specific terms, for example, the gene name.

13.2 Add clinical associations to a report

To add a single clinical association to a report, click the ***Add to report*** button in the ***Clinical association details*** panel.

Alternatively, you can add multiple clinical associations in a batch:

1. Check the applicable checkboxes.

   Hover over a clinical association to reveal a checkbox. Check individual clinical associations or select them all by clicking the ***Select all*** button.
2. Select ***Add selection to report***.

13 Operating instructions (continued)

3. (Optional) Under ***NOTES***, you can add a comment detailing why you added the clinical association to the report.
4. If necessary, check or uncheck the supporting variants checkboxes.

   Uncheck the supporting variants that are not relevant.
5. Click ***Add to report***.

If a biomarker is supported by more than one detected variant, you can choose to report:

- The clinical association in the context of one variant, or another, or
- all linked variants (at least one variant must be selected).

If a biomarker is supported by one variant only, there is no option to change the selection.

When one or more clinical associations are added to the report, the report summary section (***MY REPORT***) is updated to reflect the number of reported associations. For more information, refer to "MY REPORT" on page 22.

13.3 Generate a report

To generate a report:

1. From the interpretation project in SOPHiA DDM, click ***Preview report***.
2. Click ***Open***.

   The Report Generator application opens in your browser.

The ***Report preview*** page offers PDF preview functionalities that allow you to:

- Navigate on the report
- Print
- Download the PDF or JSON file

  ▶ For more information, refer to "Download a report" in the Report Generator User manual .

14 OncoPortal Plus updates and versioning

To access the versions of OncoPortal Plus web application and the JAX-CKB database, click on the OncoPortal Plus logo.

The JAX-CKB database version and clinical annotation process are fixed for a particular analysis. The clinical annotation process is reflected by the pipeline version, which can be found next to OncoPortal Plus and JAX-CKB versions. For example, an analysis run on 01 December 2021 will have molecular profiles, clinical associations, and clinical trials present in the database version that was available on that date.

A pipeline system update does not necessarily mean that the OncoPortal Plus clinical annotation process has been updated. Please consult the SOPHiA DDM release notes.

15 Disposal information

There is no disposal information for OncoPortal Plus.

16 Maintenance

There are no maintenance requirements for OncoPortal Plus.

17 Troubleshooting

Problem	Possible cause	Solution
I can't see OncoPortal Plus data for some of my analyses.	OncoPortal Plus is only available for analyses that are run after OncoPortal Plus has been activated on your account.	

Table 10 Troubleshooting

18 Support information

SOPHiA GENETICS SA

ZA La Pièce 12,

CH-1180 Rolle, Switzerland

European Union: +41 21 561 34 75

France: +33 5 47 51 01 29

United States: +1 617 313 7957

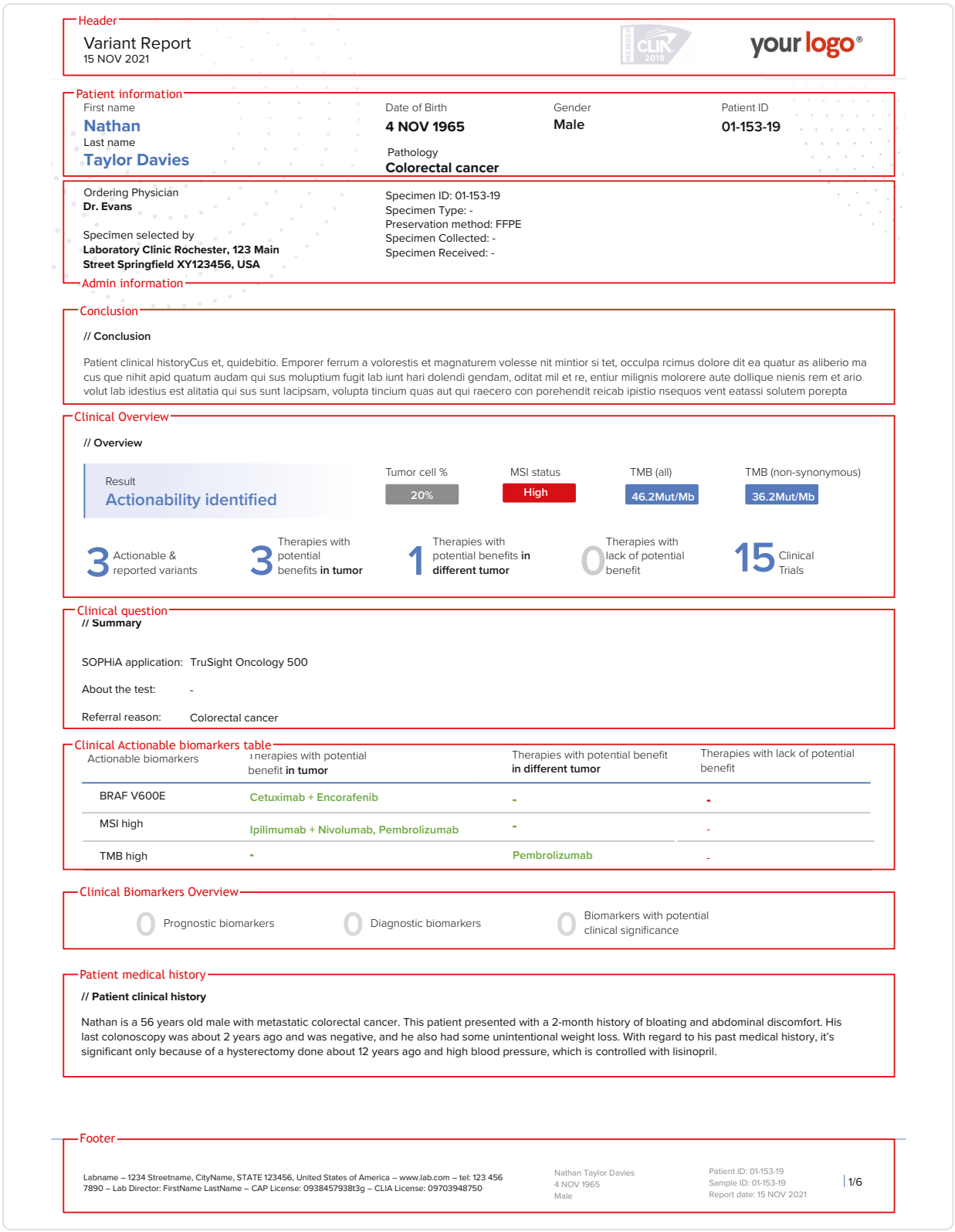
Email: support@sophiagenetics.com

Website: www.sophiagenetics.com

19 Appendix 1. Example somatic clinical report

The following pages show an example of a somatic clinical report.

19 Example somatic clinical report (continued)



Header

Variant Report
15 NOV 2021

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Patient information

First name
Nathan
Last name
Taylor Davies

Date of Birth
4 NOV 1965

Gender
Male

Patient ID
01-153-19

Pathology
Colorectal cancer

Ordering Physician
Dr. Evans

Specimen selected by
Laboratory Clinic Rochester, 123 Main Street Springfield XY123456, USA

Specimen ID: 01-153-19
Specimen Type: -
Preservation method: FFPE
Specimen Collected: -
Specimen Received: -

Admin information

Conclusion

// Conclusion

Patient clinical historyCus et, quidebitio. Emporer ferrum a volorestis et magnaturem volesse nit mintior si tet, occulpa rcimus dolore dit ea quatur as aliberio ma cus que nihit apid quatum audam qui sus moluptium fugit lab iunt hari dolendi gendam, oditat mil et re, entiur milignis molorere aute dollique nienis rem et ario volut lab idestius est alitatia qui sus sunt lacipsam, volupta tincium quas aut qui raecero con porehendit reicab ipistio nsequos vent eatassi solutem porepta

Clinical Overview

// Overview

Result
Actionability identified

Tumor cell %: 20%
MSI status: High
TMB (all): 46.2Mut/Mb
TMB (non-synonymous): 36.2Mut/Mb

3 Actionable & reported variants
3 Therapies with potential benefits **in tumor**
1 Therapies with potential benefits **in different tumor**
0 Therapies with lack of potential benefit
15 Clinical Trials

Clinical question

// Summary

SOPHiA application: TruSight Oncology 500

About the test: -

Referral reason: Colorectal cancer

Clinical Actionable biomarkers table

Actionable biomarkers	Therapies with potential benefit **in tumor**	Therapies with potential benefit **in different tumor**	Therapies with lack of potential benefit
BRAF V600E	Cetuximab + Encorafenib	-	-
MSI high	Ipilimumab + Nivolumab, Pembrolizumab	-	-
TMB high	-	Pembrolizumab	-

Clinical Biomarkers Overview

0 Prognostic biomarkers
0 Diagnostic biomarkers
0 Biomarkers with potential clinical significance

Patient medical history

// Patient clinical history

Nathan is a 56 years old male with metastatic colorectal cancer. This patient presented with a 2-month history of bloating and abdominal discomfort. His last colonoscopy was about 2 years ago and was negative, and he also had some unintentional weight loss. With regard to his past medical history, it's significant only because of a hysterectomy done about 12 years ago and high blood pressure, which is controlled with lisinopril.

Footer

Labname – 1234 Streetname, CityName, STATE 123456, United States of America – www.lab.com – tel: 123 456 7890 – Lab Director: FirstName LastName – CAP License: 0938457938t3g – CLIA License: 09703948750

Nathan Taylor Davies
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Male

Patient ID: 01-153-19
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19 Example somatic clinical report (continued)

Variant Report
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Reported variants

// Reported variants

Actionable variants in patient's tumor type

BRAF NM_004333.5:c.1799T>A, p.(Val600Glu) — BRAF V600E

Variant fraction	Coding consequence	Genomic position	Classification	Association type
16.5%	**missense**	**GRCh37/hg19**	**Pathogenic**	**Therapeutic**
Exon	Depth	**Chr7:140453136**	ClinVar	AMP/ASCO/CAP Classification
15	**2208**		**Drug response**	**IA**
			rs1219913440	

Actionable variants in different tumor type

None reported

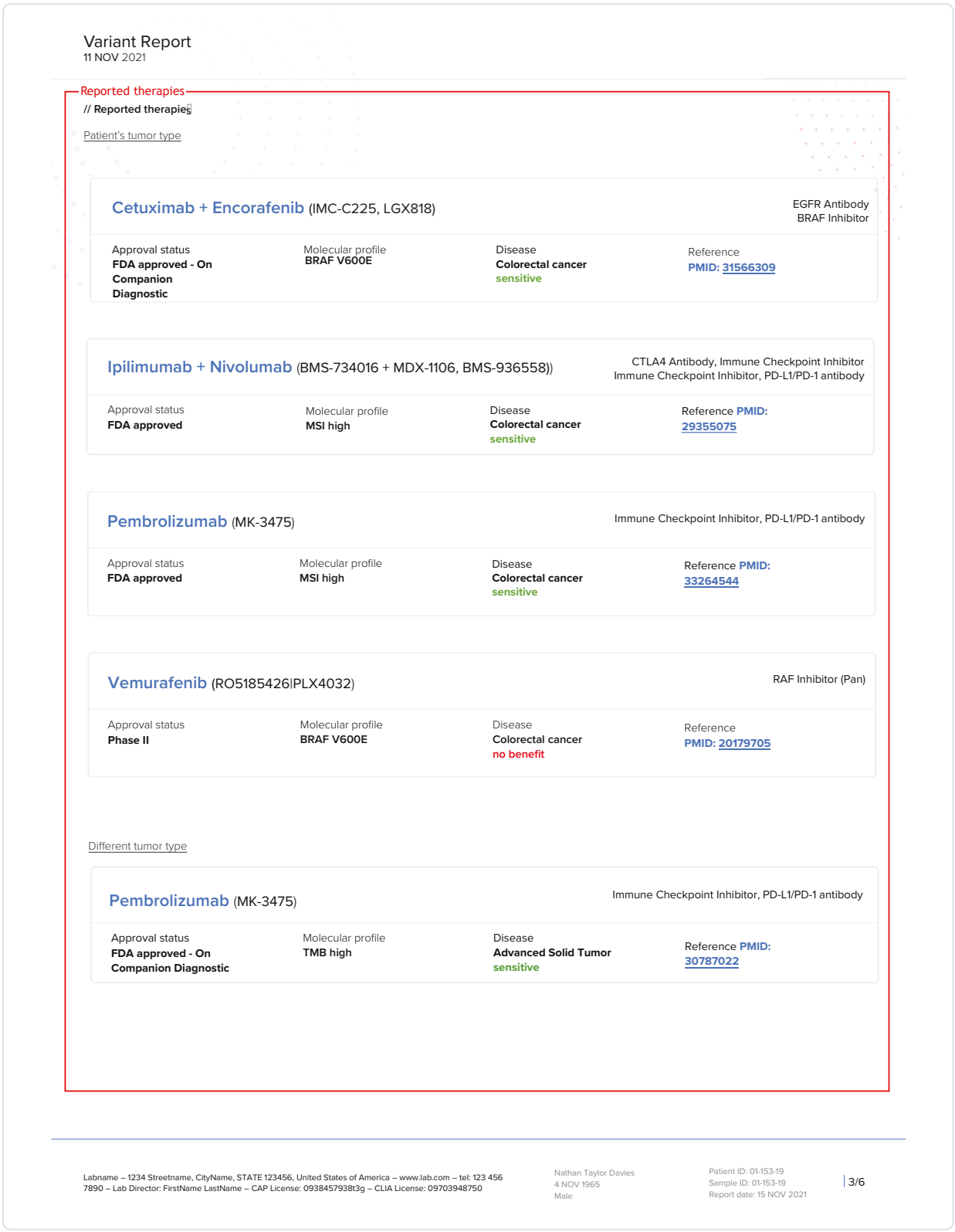
Other variants with potential clinical significance

None reported

// Other reported variants

None reported

19 Example somatic clinical report (continued)



Variant Report
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Reported therapies
// Reported therapies

Patient's tumor type

Cetuximab + Encorafenib (IMC-C225, LGX818) — EGFR Antibody, BRAF Inhibitor

Approval status	Molecular profile	Disease	Reference
FDA approved - On Companion Diagnostic	**BRAF V600E**	**Colorectal cancer** sensitive	**PMID: 31566309**

Ipilimumab + Nivolumab (BMS-734016 + MDX-1106, BMS-936558)) — CTLA4 Antibody, Immune Checkpoint Inhibitor, Immune Checkpoint Inhibitor, PD-L1/PD-1 antibody

Approval status	Molecular profile	Disease	Reference
FDA approved	**MSI high**	**Colorectal cancer** sensitive	**PMID: 29355075**

Pembrolizumab (MK-3475) — Immune Checkpoint Inhibitor, PD-L1/PD-1 antibody

Approval status	Molecular profile	Disease	Reference
FDA approved	**MSI high**	**Colorectal cancer** sensitive	**PMID: 33264544**

Vemurafenib (RO5185426|PLX4032) — RAF Inhibitor (Pan)

Approval status	Molecular profile	Disease	Reference
Phase II	**BRAF V600E**	**Colorectal cancer** no benefit	**PMID: 20179705**

Different tumor type

Pembrolizumab (MK-3475) — Immune Checkpoint Inhibitor, PD-L1/PD-1 antibody

Approval status	Molecular profile	Disease	Reference
FDA approved - On Companion Diagnostic	**TMB high**	**Advanced Solid Tumor** sensitive	**PMID: 30787022**

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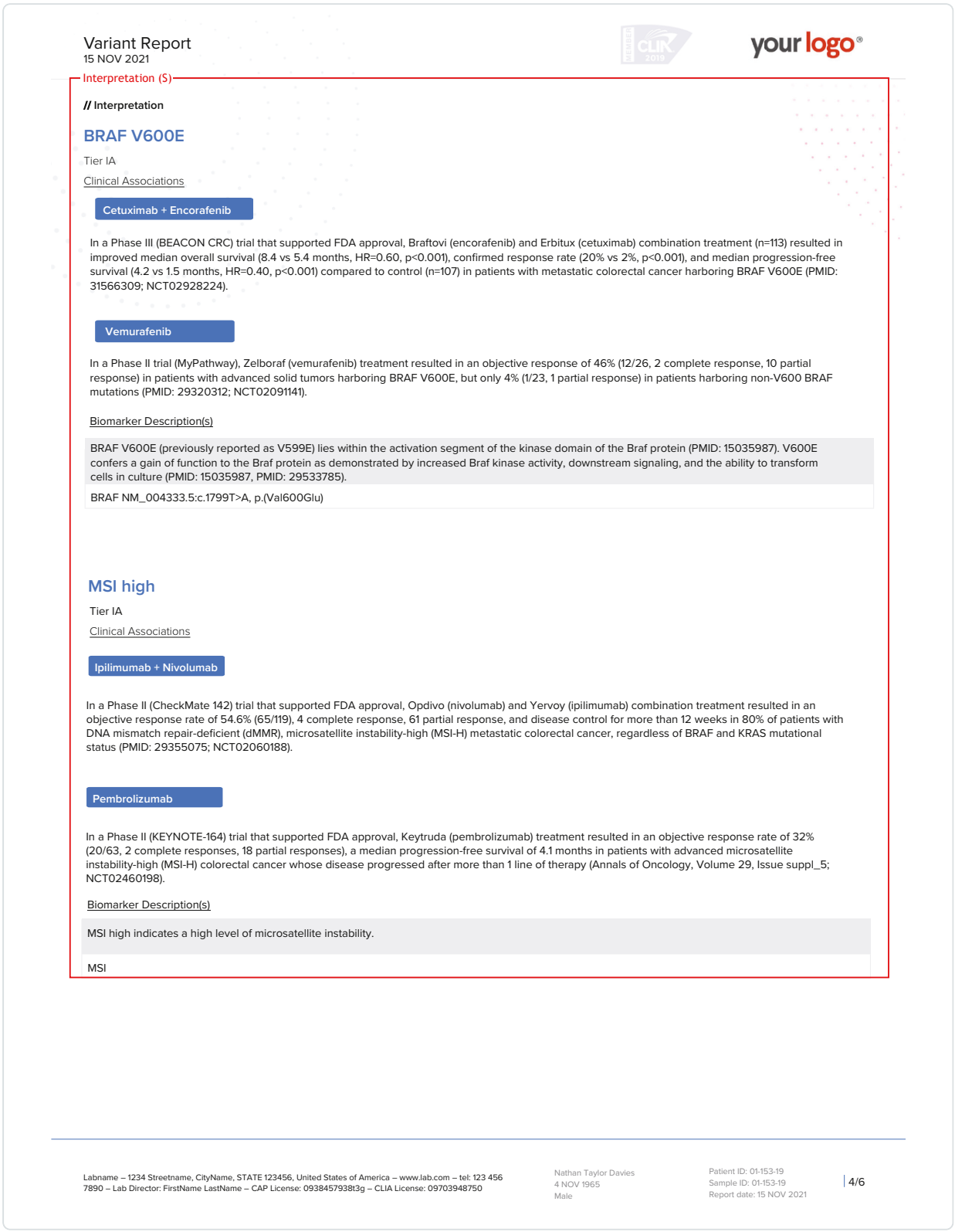
19 Example somatic clinical report (continued)



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Interpretation (S)

// Interpretation

BRAF V600E

Tier IA

Clinical Associations

Cetuximab + Encorafenib

In a Phase III (BEACON CRC) trial that supported FDA approval, Braftovi (encorafenib) and Erbitux (cetuximab) combination treatment (n=113) resulted in improved median overall survival (8.4 vs 5.4 months, HR=0.60, p<0.001), confirmed response rate (20% vs 2%, p<0.001), and median progression-free survival (4.2 vs 1.5 months, HR=0.40, p<0.001) compared to control (n=107) in patients with metastatic colorectal cancer harboring BRAF V600E (PMID: 31566309; NCT02928224).

Vemurafenib

In a Phase II trial (MyPathway), Zelboraf (vemurafenib) treatment resulted in an objective response of 46% (12/26, 2 complete response, 10 partial response) in patients with advanced solid tumors harboring BRAF V600E, but only 4% (1/23, 1 partial response) in patients harboring non-V600 BRAF mutations (PMID: 29320312; NCT02091141).

Biomarker Description(s)

BRAF V600E (previously reported as V599E) lies within the activation segment of the kinase domain of the Braf protein (PMID: 15035987). V600E confers a gain of function to the Braf protein as demonstrated by increased Braf kinase activity, downstream signaling, and the ability to transform cells in culture (PMID: 15035987, PMID: 29533785).
BRAF NM_004333.5:c.1799T>A, p.(Val600Glu)

MSI high

Tier IA

Clinical Associations

Ipilimumab + Nivolumab

In a Phase II (CheckMate 142) trial that supported FDA approval, Opdivo (nivolumab) and Yervoy (ipilimumab) combination treatment resulted in an objective response rate of 54.6% (65/119), 4 complete response, 61 partial response, and disease control for more than 12 weeks in 80% of patients with DNA mismatch repair-deficient (dMMR), microsatellite instability-high (MSI-H) metastatic colorectal cancer, regardless of BRAF and KRAS mutational status (PMID: 29355075; NCT02060188).

Pembrolizumab

In a Phase II (KEYNOTE-164) trial that supported FDA approval, Keytruda (pembrolizumab) treatment resulted in an objective response rate of 32% (20/63, 2 complete responses, 18 partial responses), a median progression-free survival of 4.1 months in patients with advanced microsatellite instability-high (MSI-H) colorectal cancer whose disease progressed after more than 1 line of therapy (Annals of Oncology, Volume 29, Issue suppl_5; NCT02460198).

Biomarker Description(s)

MSI high indicates a high level of microsatellite instability.
MSI

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19 Example somatic clinical report (continued)

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TMB high

Tier IA

Clinical Associations

Pembrolizumab

In a retrospective analysis of a Phase II trial (KEYNOTE-158) that supported FDA approval, Keytruda (pembrolizumab) treatment resulted in superior objective response rate (28.3% vs 6.5%) in adult and pediatric patients with TMB high (TMB >= 10 mut/Mb, n=120) advanced solid tumors compared to patients with TMB low (TMB < 10 mut/Mb, n=635) tumors (Ann Oncol, 30 (Suppl 5), Oct 2019, v477-v478; NCT02628067).

Biomarker Description(s)

TMB high indicates a high tumor mutational burden.
TMB

Gene description(s)

BRAF

BRAF, serine/threonine-protein kinase B-raf, is a member of the Raf family of serine/threonine protein kinases, which signals through the MAP kinase pathway to regulate cell proliferation and cell growth (PMID: 24737949, PMID: 29540830). BRAF mutations and fusions have been identified in a variety of cancers, including, colorectal (PMID: 30122982), lung (PMID: 29729495), thyroid (PMID: 12970315), and melanoma (PMID: 24737949), and a number of mutations have also been demonstrated to confer drug resistance (PMID: 27478040).

MSI

MSI, Microsatellite Instability

TMB

TMB, Tumor Mutational Burden

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19 Example somatic clinical report (continued)

Variant Report
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Methodology

// **Methodology**

SOPHiA application
TSO500
SOPHiA DDM
5.10.4--b131-b74ec54
Pipeline ID/Revision number/Splitting ID
LL1XG1G2_CNV_exome_1 / v5.5.34 / GEN1GN1FSQ2

Reference genome
GRCh37/hg19
Sequencer
Illumina MiSeq

Run date
15.11.2021
Run name
Oncology Application
Analysis ID
200240322
MID
S21

Methodology

Somatic gene variant annotations and related content have been powered by, without limitation, The Jackson Laboratory Clinical Knowledgebase (JAX-CKB™).

Classification disclaimer

Variant classifications present in the report are the responsibility of the report author and approver.

Analysed by / Validated by

Signature

Analyzed by **Marian Novak**

Date 15.11.2021

Signature

Labname – 1234 Streetname, CityName, STATE 123456, United States of America – www.lab.com – tel: 123 456 7890 – Lab Director: FirstName LastName – CAP License: 0938457938t3g – CLIA License: 09703948750

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19 Example somatic clinical report (continued)

Variant Report
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Annexe - Retained Variants

// SNVs/INDELs (retained)

Variant	Exon	Variant fraction	Coding consequence	Classification	ClinVar
CDH1 NM_004360.1:c.48+6C>T,-	1	99.9%	Intronic	Likely pathogenic	Benign rs3743674
BRCA2 NM_000049.3:c.739T>C,p.(Val2466Ala)	14	100%	missense	Definitely pathogenic	- -
MPZ NM_00530.7:c.532del,-	3	99.9%	Intronic	Likely benign	Benign rs379999

Annexe - Retained Fusions

// Fusions (retained)

Fused genes 5'-3'	Exons 5'-3'	Read count Supporting reads	Unique molecule count Supporting unique molecules	cDNA sequence 5'-3'
TMPRSS2 - ERG	1 - 2	686 93.6%	127 51.6%	CTGCGCAAAGCCAGCGTGACCATC GAGGATCCAAAGTGGGAATTCCCT
FGFR3 - TACC3	17 - 11	235 23.5%	91 52.0%	CTGCGCAAAGCCAGCGTGACCATC GAGGATCCAAAGTGGGAATTCCCT
ETV6 - NTRK3	5 - 15	374 100.0%	105 100.0%	CTGCGCAAAGCCAGCGTGACCATC GAGGATCCAAAGTGGGAATTCCCT
NCOA4 - RET	8 - 12	445 52.6%	93 67.4%	CTGCGCAAAGCCAGCGTGACCATC GAGGATCCAAAGTGGGAATTCCCT
EGFR - EGFR	1 - 8	680 43.2%	131 78.4%	CTGCGCAAAGCCAGCGTGACCATC GAGGATCCAAAGTGGGAATTCCCT

Annexe - Low Confidence Variants

// SNVs/INDELs (low confidence)

Variant	Exon	Variant fraction	Coding consequence	Classification	ClinVar
CDH1 NM_004360.1:c.48+6C>T,-	1	99.9%	Intronic	Likely pathogenic	Benign rs3743674
BRCA2 NM_000049.3:c.739T>C,p.(Val2466Ala)	14	100%	missense	Definitely pathogenic	- -
MPZ NM_00530.7:c.532del,-	3	99.9%	Intronic	Likely benign	Benign rs379999

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Nathan Taylor Davies
4 NOV 1965
Male

Patient ID: 01-153-19
Sample ID: 01-153-19
Report date: 15 NOV 2021

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19 Example somatic clinical report (continued)

Variant Report
15 NOV 2021

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Annexe - Filtering strategy

// Filtering strategy (for reported variants)

Variant	Filter type	Description
CDH1 NM_004360:c.48+6C>T,-	CASCADE	ACMG score: Pathogenic OR Likely pathogenic OR Uncertain significance
BRCA2 NM_000049:c.739T>C,p.(Val2466Ala)	SOPHIA	RETAINED Retained variants
MPZ NM_00530.7:c.532del,-	SOPHIA	RETAINED Retained variants

Labname – 1234 Streetname, CityName, STATE 123456, United States of America – www.lab.com – tel: 123 456 7890 – Lab Director: FirstName LastName – CAP License: 0938457938t3g – CLIA License: 09703948750

Nathan Taylor Davies
4 NOV 1965
Male

Patient ID: 01-153-19
Sample ID: 01-153-19
Report date: 15 NOV 2021

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Document Approvals

Approved Date: 01 Feb 2024

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Approval Verdict: Approve	Pierre Naibo, (pnaibo@sophiagenetics.com) Management Approval 30-Jan-2024 15:30:23 GMT+0000

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