OncoPortal™ Plus

APP NOTE

SOPHiA GENETICS™

Streamline clinical interpretation of comprehensive genomic profiling with OncoPortal™ Plus

Comprehensive genomic profiling (CGP) of tumors using next-generation sequencing (NGS) is increasingly being used to aid decision making. These broad sequencing panels have the potential to identify more possible treatment targets than smaller panels, but generate hundreds of variants so that pinpointing actionable information is challenging. Complex molecular profiles of SNVs/Indels, copy number variations (CNVs), fusions, microsatellite instability (MSI) status and tumor mutational burden (TMB) need to be consistently, accurately, and efficiently interpreted without missing key actionable insights. The key findings then need to be summarized in a comprehensive genomic report that can be customized to individual preferences and standards.

OncoPortal™ Plus is an evidence-based decision support software fully integrated into the SOPHiA DDM™ workflow to aid the interpretation of genomic variants identified through NGS assays (Figure 1). SOPHiA DDM™ automatically detects, annotates, and pre-classifies genomic variants from raw sequencing data. Subsequently, the user-friendly OncoPortal™ Plus web application, exclusively accessible through SOPHiA DDM™, characterizes biomarkers associated with specific solid and hematological malignancies and their Clinical Associations (including available therapies, clinical trials, diagnosis, and prognosis) using published literature and guidelines. Finally, laboratories can customize state-of-the-art comprehensive genomic and genetic reports using an unlimited number of customizable templates to address their unique needs.

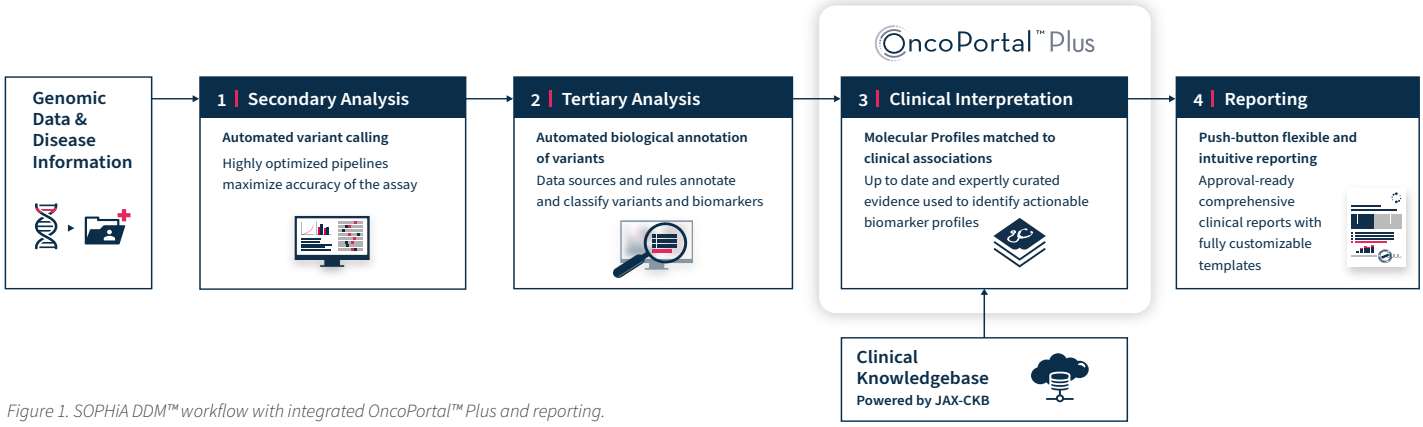

Figure 1. SOPHiA DDM™ workflow with integrated OncoPortal™ Plus and reporting.

Here, we will demonstrate the power of OncoPortal™ Plus for the interpretation of genomic data obtained with SOPHiA DDM™ for TruSight® Oncology 500 (TSO500). TSO500 is a CGP assay that profiles >500 genes to detect multiple variant types and complex biomarkers such as MSI and TMB. OncoPortal™ Plus is able to identify variants (biomarkers) and their Clinical Associations from SOPHiA DDM™ for TSO500, facilitating the generation of detailed and intuitive reports to support decision making.

1. Starting variant interpretation in the SOPHiA DDM™ Platform

When accessing SOPHiA DDM™, all available applications (bioinformatic workflows) are displayed on the Dashboard (Figure 2). When SOPHiA DDM™ has completed the TSO500 sequencing analysis, users receive an email notification to securely log in and begin the interpretation. Clicking on “TruSight Oncology500” provides access to the TSO500 workspace.

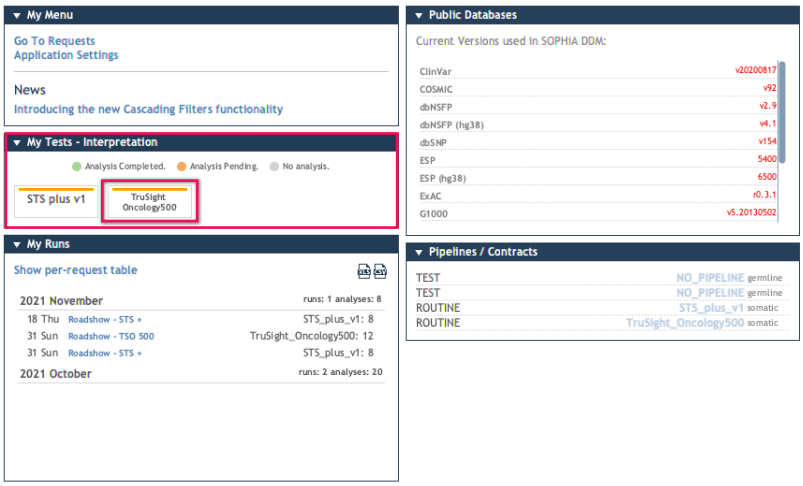

Figure 2. SOPHiA DDM™ home screen displaying all available applications.

2. Initiating a new interpretation project

The TSO500 workspace automatically displays all available runs and samples, ready for interpretation. To start the assessment of Sample 01-153-19, we create a “New Interpretation Project”. First, click “add interpretation”, select the disease from a drop-down menu (in this case “Colorectal cancer”), give the interpretation a name, and click “Finish” (Figure 3).

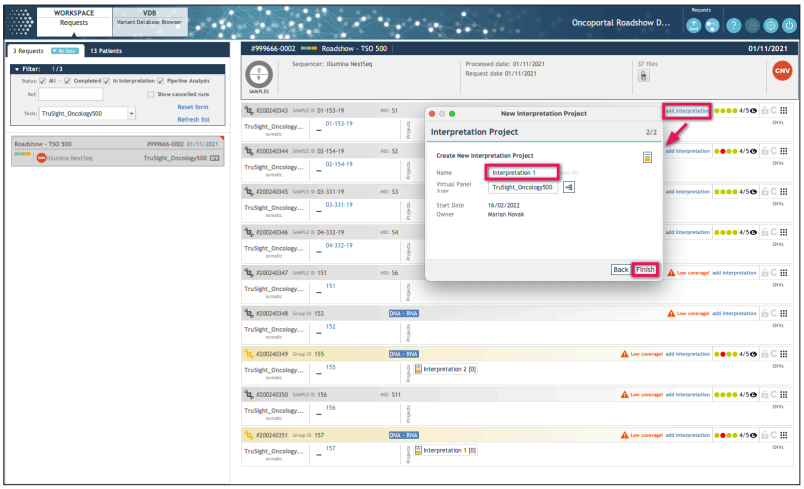

Figure 3. SOPHiA DDM™ TSO500 workspace, and initiation of a new interpretation project for the selected sample.

3. Viewing an overview of a sample’s genomic variants

After creating a new interpretation project, the platform offers a glimpse of the detected variants in the “Overview” tab (Figure 4). This tab provides a high-level summary of the findings, including the number of variants, retained variants, MSI status, and TMB.

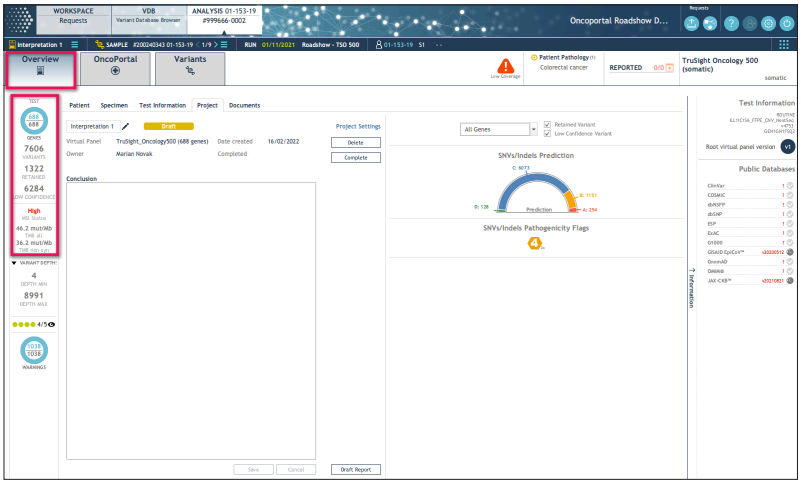

Figure 4. SOPHiA DDM™ Overview tab for the selected sample.

4. Accessing OncoPortal™ Plus through SOPHiA DDM™

There are two ways to review SNVs/Indels, fusions, and CNVs. The variants can be reviewed individually in the "Variants" tab in SOPHiA DDM™, or the results can be interpreted using OncoPortal™ Plus by clicking on the "OncoPortal" tab. Clicking on "OncoPortal" will display a pop-up that gives the option to access the "NEW OncoPortal web app!" or "Legacy OncoPortal" (Figure 5). We will explore OncoPortal™ Plus through the new OncoPortal web app.

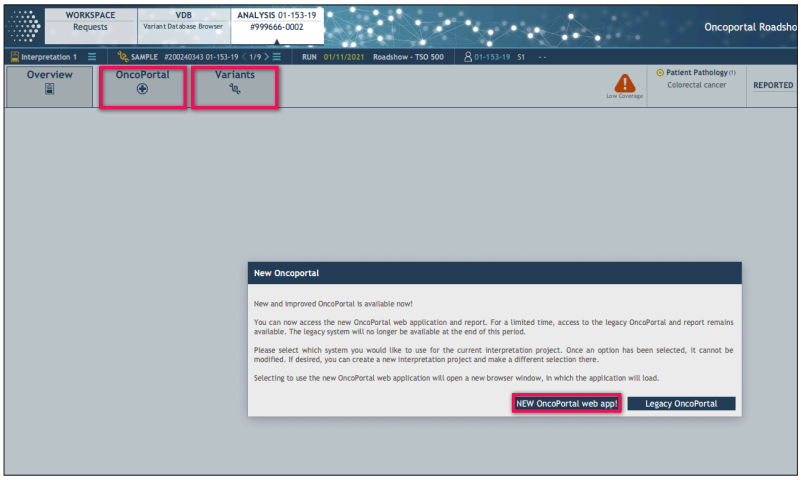

Figure 5. Access to OncoPortal™ Plus via SOPHiA DDM™.

5. Viewing Molecular Profiles in the OncoPortal™ Plus web application

OncoPortal™ Plus opens as a new web browser window. Information flows securely between the SOPHiA DDM™ Platform and the web application, so that the top panel of OncoPortal™ Plus is automatically populated with the same case details as in SOPHiA DDM™ (Figure 6). Viewing OncoPortal™ Plus in a web browser allows multiple projects to be opened at the same time, in different tabs.

The web application has a range of intuitive features. On the left-hand side, it is possible to switch between "Molecular Profiles" and "Clinical Trials" views. The "Molecular Profiles" view is a key feature of OncoPortal™ Plus. Molecular Profiles detail interactions between co-occurring biomarkers, which are listed in the main table. This display captures the potential biological interaction of different biomarkers present in the same sample. For example, one biomarker might indicate sensitivity to a targeted agent, whereas another co-occurring biomarker might indicate resistance to the same agent. Rather than considering each variant individually, this feature supports the assessment of the relationship between multiple tumor alterations and their compound impact on therapeutic efficacy, diagnosis, prognosis, or access to clinical trials.

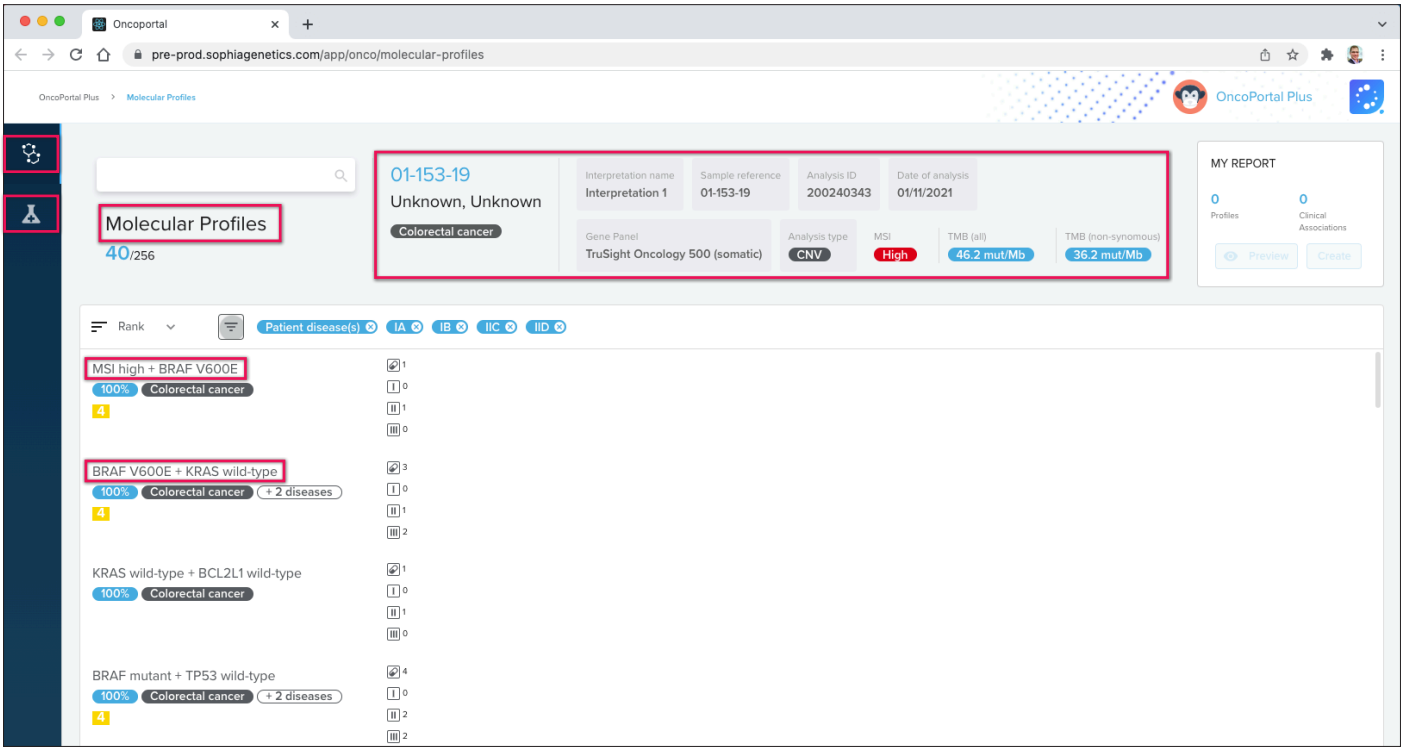

Figure 6. OncoPortal™ Plus web application Molecular Profiles display for a selected sample.

6. Filtering Molecular Profiles

A useful feature in OncoPortal™ Plus is the ability to filter the results and focus on the most actionable information first. Filters include cancer type (disease), AMP/ASCO/CAP tier, association type, approval authority (FDA, EMA, TGA), and response type (therapy, diagnosis, prognosis) (Figure 7). After filtering, it is possible to rank the results in different orders, according to preference.

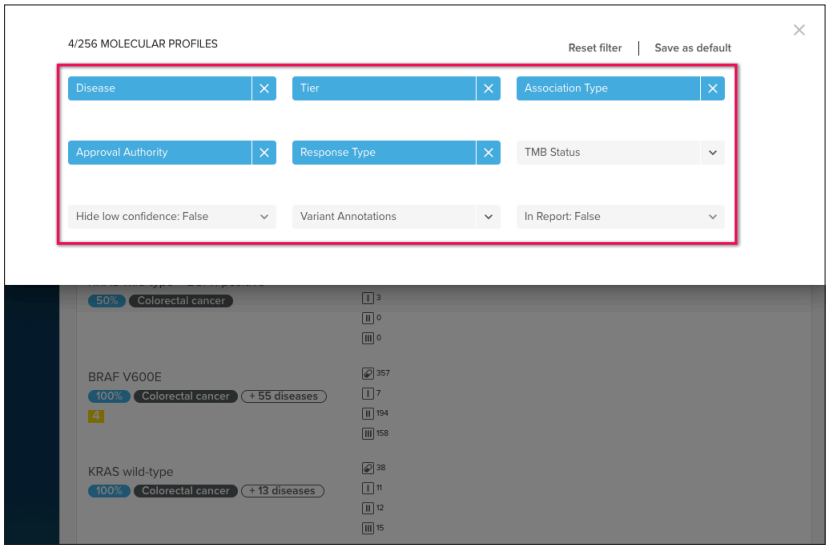

Figure 7. Filtering feature in OncoPortal™ Plus.

7. Exploring Molecular Profiles

After filtering and ranking, in this example, the number of Molecular Profiles was narrowed down from 256 to 5. *BRAF* V600E was identified as the most relevant variant (Figure 8). To explore this biomarker in more detail, click on the associated Molecular Profile and then click "ⓘ" next to the variant name. This displays rich interpretive information related to both normal gene function and biomarker function, supported by up-to-date scientific sources.

We also see a list of Clinical Associations related to the *BRAF* V600E Molecular Profile in the main table. The labels on the right enable a quick review of the key details, such as whether the biomarker is sensitive or resistant to the targeted agent, therapy approval status, clinical trial phase, and AMP/ASCO/CAP tier/evidence level.

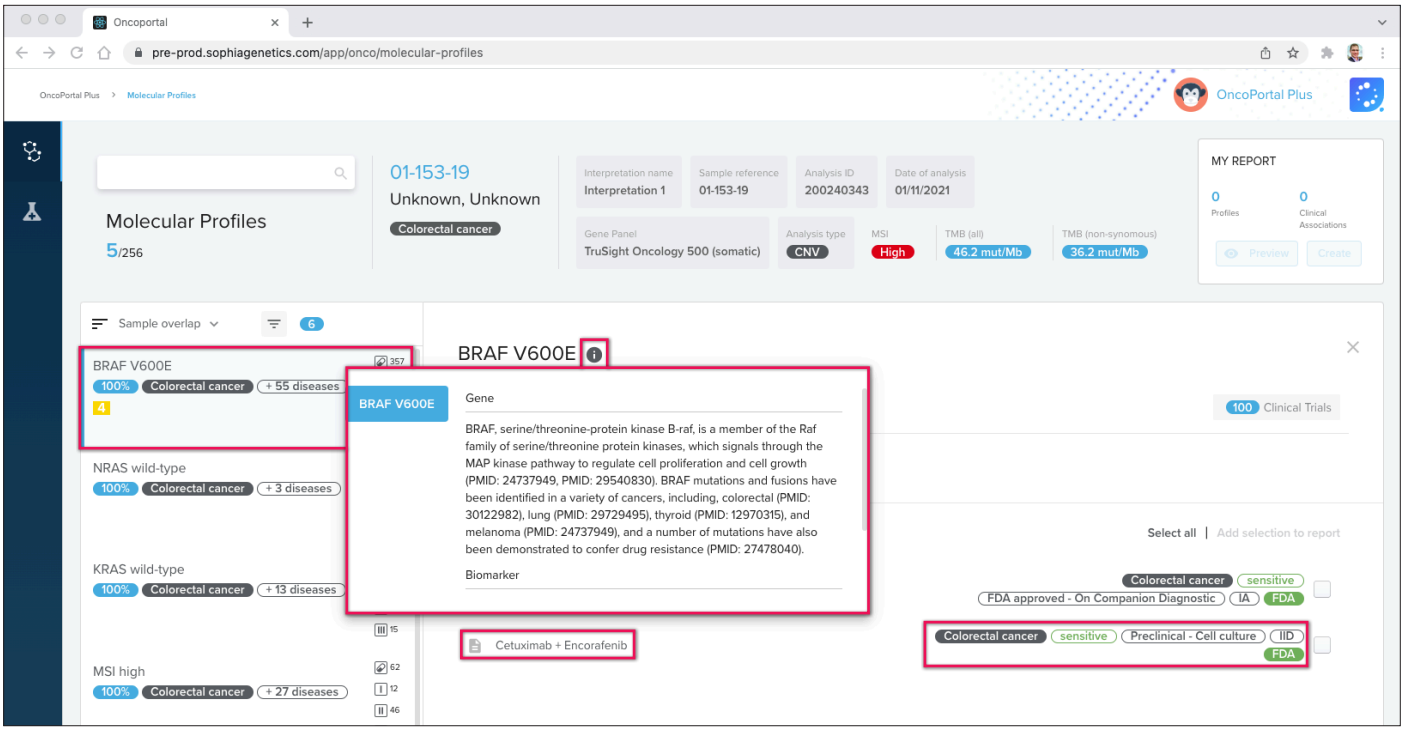

Figure 8. Further exploration of the BRAF V600E Molecular Profile in OncoPortal™ Plus.

8. Gaining additional insights into Clinical Associations for a given biomarker

Clicking on a Clinical Association reveals additional details, such as the mechanism of action of a given drug (Figure 9). Molecular Profiles can be added to the report by selecting the Clinical Association of interest and checking the “Add selection to report” box, or by clicking the “Add to report” button when viewing the Clinical Association. The entry can be customized with a user-entered note, e.g., to explain why a specific Molecular Profile and Clinical Association have been selected.

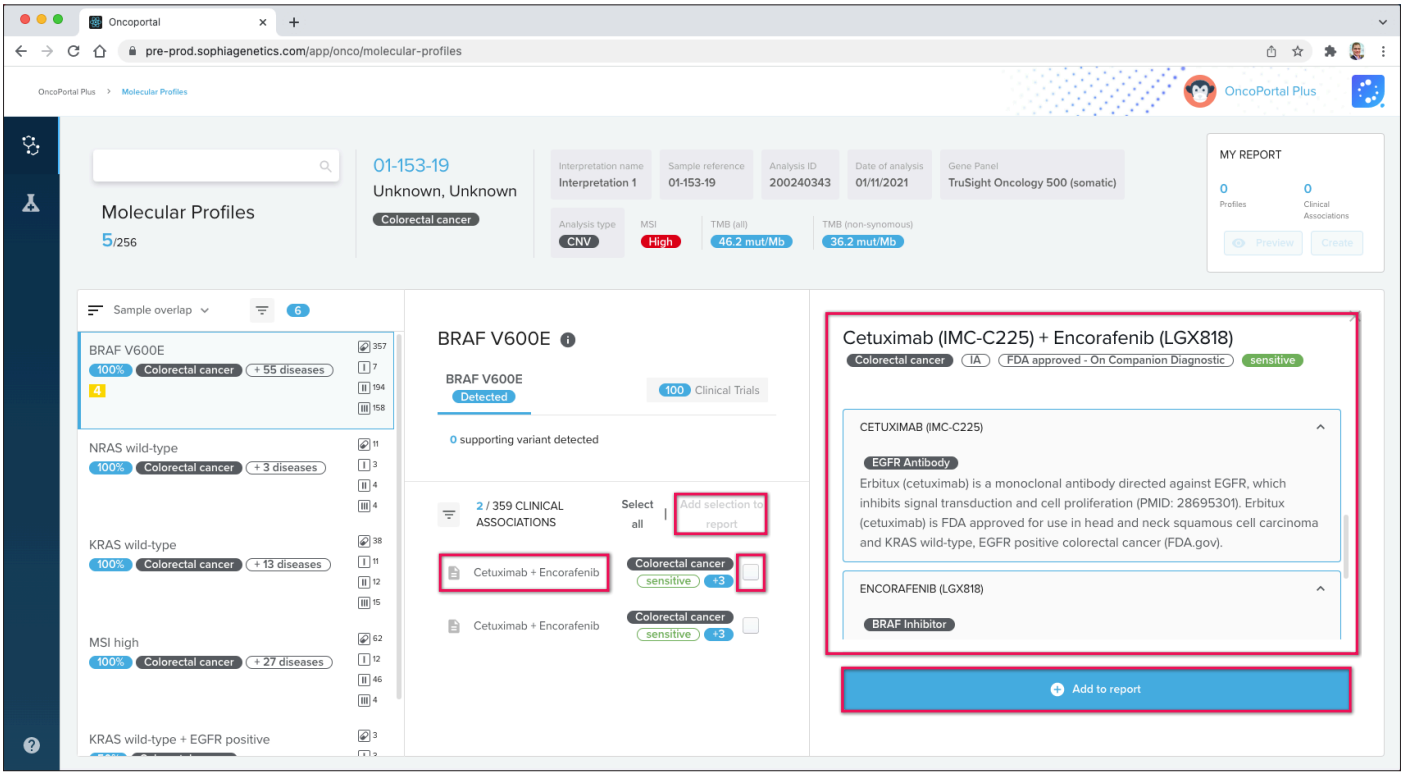

Figure 9. Further details about Clinical Associations and adding items to the OncoPortal™ Plus report.

9. Customizing templates for comprehensive reports

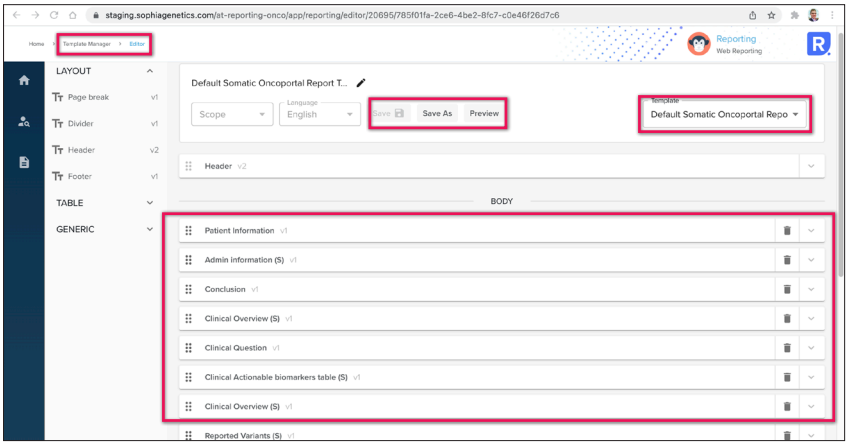

Figure 10. The SOPHiA DDM™ Template Manager Editor for configuring custom reporting templates.

In SOPHiA DDM™, the Template Manager provides a user-friendly interface for the preparation of custom reporting templates (Figure 10). First, we select one of the provided templates. Then, the Editor can be used to activate/deactivate, rename, and configure individual report sections (stencils) with granular information fields. The final customized template can be previewed and saved, and then used for subsequent reports.

10. Completing a comprehensive genomic report

During the clinical interpretation, information flows securely between OncoPortal™ Plus and SOPHiA DDM™, so that after selecting Molecular Profiles and Clinical Associations in OncoPortal™ Plus, the report can be completed in the SOPHiA DDM™ Overview tab (Figure 11), where the case information can be edited, and the Conclusion written. The 'Complete' button launches the web-based Reporting app (Figure 12), where a previously configured template can be selected. The reporting app populates the template with the case, biomarker, and interpretive information from OncoPortal™ Plus and SOPHiA DDM™. Approval of the final report can then be initiated from the reporting app, so that the approver is notified that the report is ready for review and approval.

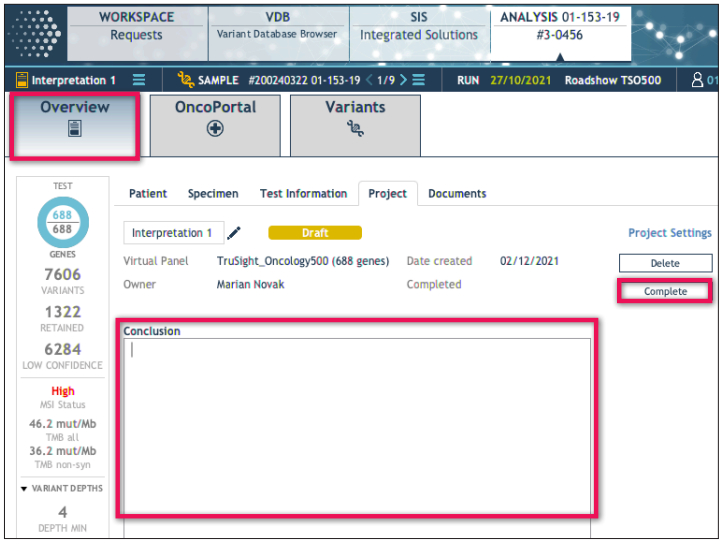

Figure 11. The SOPHiA DDM™ Overview tab for completion of the report.

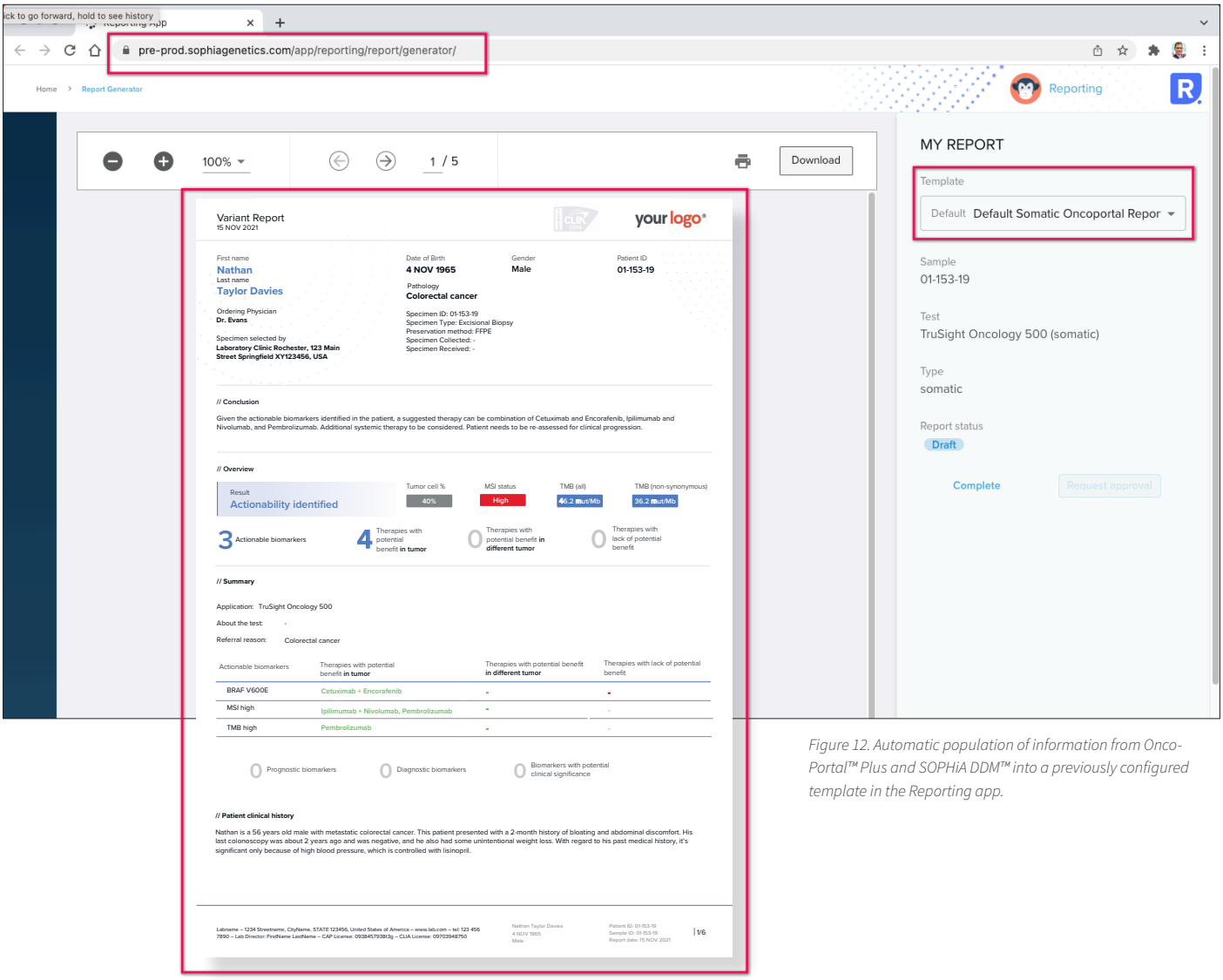

Figure 12. Automatic population of information from OncoPortal™ Plus and SOPHiA DDM™ into a previously configured template in the Reporting app.

Conclusion

OncoPortal™ Plus is a user-friendly module of SOPHiA DDM™, integrated into the platform's streamlined sample-to-report workflow. The OncoPortal™ Plus web application intuitively displays and reviews co-occurring biomarkers as Molecular Profiles, to reduce the chance of missing interfering variants and speed up interpretation. Molecular Profiles can be filtered to display the most actionable biomarker first, further streamlining assessment. OncoPortal™ Plus provides detailed descriptions of gene and biomarker functions, and rich information to support the Clinical Associations between Molecular Profiles and therapeutic options, clinical trials, diagnosis, and prognosis of specific cancer types, using up-to-date published scientific sources.

OncoPortal™ Plus gives users the confidence to make fast decisions with consistent and accurate interpretation of clinically significant biomarkers. Users are able to save time and reduce errors from manual interpretation of comprehensive data sets like the TSO500 CGP, and can efficiently communicate results via customizable, comprehensive, state-of-the-art reports generated in SOPHiA DDM™.

About SOPHiA GENETICS

SOPHiA GENETICS (Nasdaq: SOPH) is a healthcare technology company dedicated to establishing the practice of data-driven medicine as the standard of care and for life sciences research. It is the creator of the SOPHiA DDM™ platform, a cloud-based SaaS platform capable of analyzing data and generating insights from complex multimodal data sets and different diagnostic modalities. The SOPHiA DDM™ platform and related solutions, products and services are currently used by more than 780 hospital, laboratory, and biopharma institutions globally.

Want to know more?

Contact us at:

info@sophiagenetics.com

OncoPortal™ Plus is for Clinical Decision Support Use Only - Not intended as a primary diagnostic tool.
SOPHiA DDM™ for TSO500 is for Research Use Only and is not intended for purposes other than research. SOPHiA DDM™ for TSO500 is not for diagnostic, therapeutic, or treatment purposes.