Comprehensive Genomic Profiling using VarSome Clinical & Twist

Benchmarking of Variant Analysis and TMB & MSI

Introduction

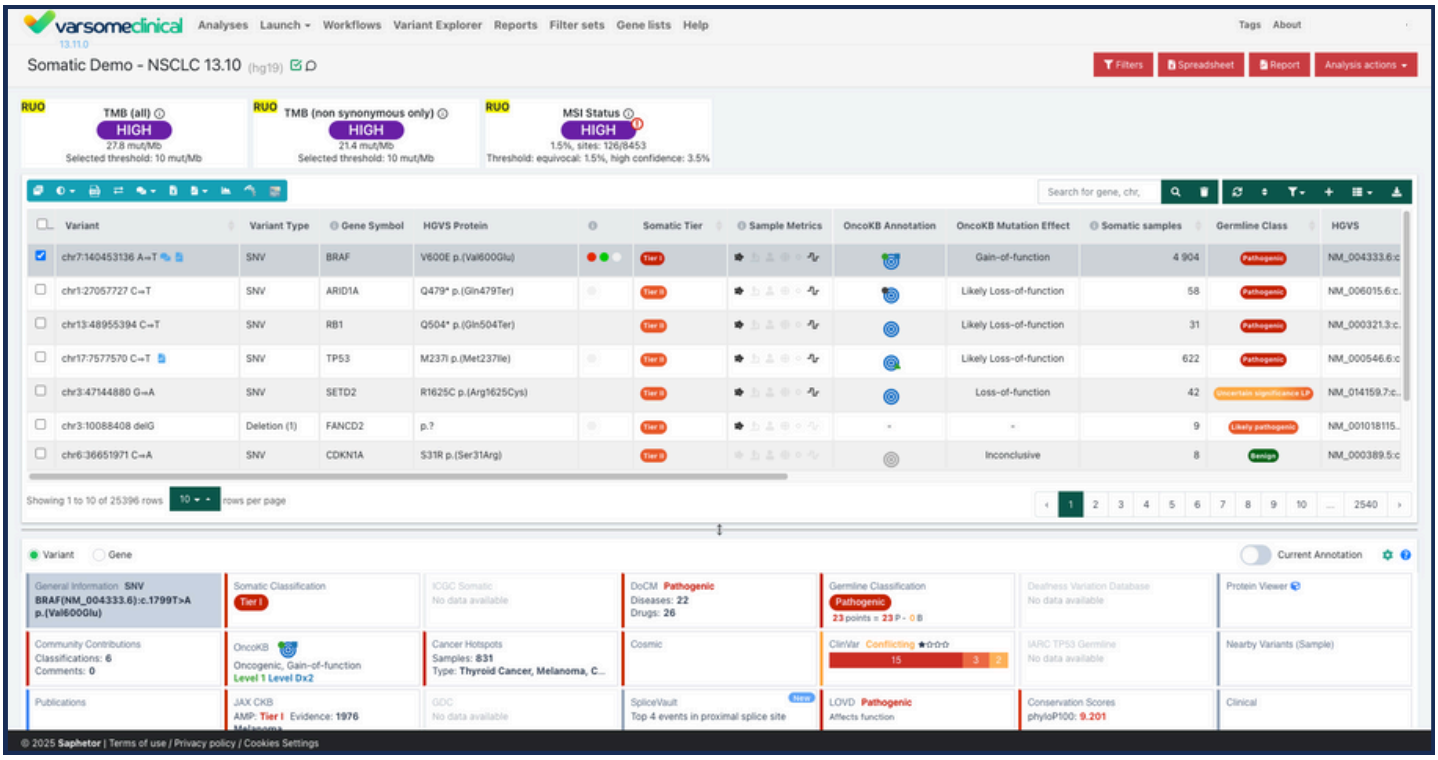
Comprehensive Genomic Profiling (CGP) panels consolidate multiple tumor biomarkers into a single assay, reducing the need for multiple targeted panels or testing modalities. **We evaluated the Twist Oncology DNA CGP panel using VarSome Clinical to assess performance across key biomarkers. Our analysis demonstrates strong concordance between expected and observed alterations, including TMB, MSI, and variant allele frequencies (VAFs) in representative reference samples.** These results highlight the robustness of Twist's assay design combined with VarSome Clinical's interpretation framework, ensuring accurate and clinically meaningful insights for oncology practice.

Twist Oncology DNA CGP Panel

The Twist Oncology DNA CGP panel (2.4 Mb) detects key variant classes, including SNVs, indels, CNVs, fusions, splice variants, and clinically relevant biomarkers such as TMB and MSI. **Covering 562 genes for SNVs, 57 for CNVs, 50 microsatellite loci, and selected DNA fusions,** the panel provides a single, broad assay for comprehensive tumour profiling.

VarSome Clinical Overview

VarSome Clinical is an IVDR-certified platform for clinical-grade variant interpretation. It supports **SNVs, indels, CNVs, structural variants, and TMB & MSI*, with support for RNA Fusions coming soon.** The platform integrates oncology-focused data sources, **including OncoKB™, JAX-CKB, and CIViC, and applies automated somatic classification based on AMP/ASCO/CAP guidelines** to provide consistent, evidence-based analysis across clinical workflows and help molecular oncology experts translate genomic data into actionable insights for patient care.



*Currently Research Use Only with IVDR Certification expected 2026.

sales@varsome.com

sales@twistbioscience.com

Methods

The Twist Oncology DNA CGP Panel (2.4 Mb) was evaluated using DNA reference standards from Horizon and SeraCare, containing SNVs, indels, CNVs, TMB, and MSI, including samples with moderately and severely fragmented DNA. Libraries were prepared according to the Twist protocol and sequenced on an Illumina platform. Each sample was analyzed in duplicate. Data were analyzed with VarSome Clinical to assess concordance of expected and observed VAFs, evaluate TMB and MSI, and confirm detection of CNVs, including amplifications.

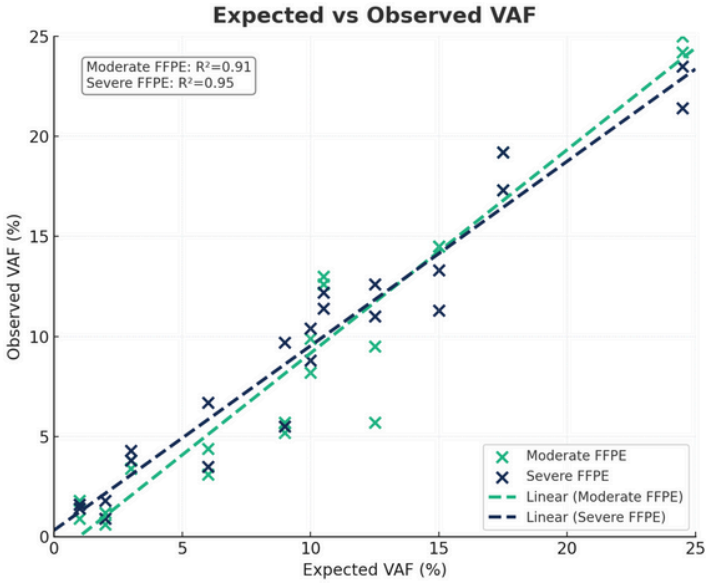


Figure 1. Concordance of expected and observed variant allele frequencies (VAFs) across Horizon reference standards. Samples included HD799 (Moderate FFPE) and HD803 (Severe FFPE). Each sample was analysed in duplicate, with observed VAFs plotted against expected values. Dashed lines represent linear regression for each sample group, demonstrating strong concordance across variant types and replicate runs.

Table 1. Sequencing performance metrics for the Twist CGP panel across all reference samples. Values are reported as averages with ranges in parentheses.

Metric	Average (Range)
Mean Target Coverage	1137.9 (336.4–1737.7)
On-Target Rate (%)	79.6% (78.0–81.0%)
Fold-80 Base Penalty (Downsampled to 32M)	1.34 (1.25–1.54)
Duplication Rate (%)	22.5% (14.0–32.4%)
% Target Bases >100x	99.6% (99.3–99.7%)

Results

Across all replicates, the observed VAFs showed strong concordance with the expected values, demonstrating the reliable detection of SNVs and indels within the Twist CGP panel. The comparison of replicates confirmed consistent performance, with minimal variation between runs. For broader genomic signatures, VarSome Clinical correctly identified the SeraCare MSI-High control as MSI-High in both replicates, and reported TMB at 26.3 mut/Mb, closely matching the expected value of 26 mut/Mb. Copy number alterations present in the reference samples, including amplifications, were also detected as expected, confirming that VarSome Clinical reliably identifies these variant classes.

Discussion

Observed VAFs showed high concordance with expected values, confirming the accuracy of the Twist CGP panel when analysed with VarSome Clinical. Results were consistent across replicates, supporting reproducibility and reliable performance. MSI-High and TMB controls were correctly identified, further demonstrating the platform's ability to estimate complex genomic signatures with precision. Current limitations include the exclusion of translocation events, which are not yet part of the validated workflow. Nonetheless, the strong agreement across variant classes and reference standards highlights the robustness of the combined assay and analysis pipeline, and its suitability for integration into clinical laboratory workflows.

Conclusions

The Twist CGP panel, analyzed with VarSome Clinical, demonstrated accurate and reproducible detection of multiple variant types and genomic signatures across reference samples. These results support its value as a reliable solution for comprehensive genomic profiling in clinical workflows. The combined performance highlights its potential to streamline validation and routine testing in oncology laboratories.