illumina®

TruSight™ Oncology Comprehensive HRD (DRAGEN™)

CE-marked under IVDR, kitted solution for accurate HRD detection

- Assess small variants, insertions, deletions, and exon-level deletions in *BRCA1* and *BRCA2* genes
- Detect genomic instability with a proprietary algorithm powered by Myriad Genetics
- Deliver an easy-to-read, clinically relevant report to help inform therapy decisions in ovarian cancer

Introduction

Precision medicine is redefining health care by leveraging the interplay between individual genetic, environmental, and lifestyle factors to create tailored therapeutic approaches.[1] In oncology, it has revolutionized care by targeting the molecular and genetic drivers of cancer, offering therapies matched to the unique genomic profiles of patients and their tumors.[2] Through advances in genomic profiling, oncologists can identify actionable biomarkers to improve therapy selection, access to clinical trials, and patient outcomes.

The genomic signature homologous recombination deficiency (HRD) results from a cell's inability to repair double-stranded DNA breaks, leading to genomic instability that drives cancer development.[3] HRD detection can play a critical role in identifying patients with ovarian cancer who may benefit from targeted therapies, specifically poly(ADP-ribose) polymerase inhibitors (PARPi).[4] By providing a CE-marked *in vitro* diagnostic (IVD) with a fully kitted workflow, TruSight Oncology Comprehensive HRD (DRAGEN) streamlines HRD testing and facilitates efficient integration into clinical laboratory processes.

HRD as a cancer biomarker

HRD is a biomarker of increasing importance in ovarian cancers.[5] The ability to repair DNA damage via the homologous recombination repair (HRR) pathway is essential for maintaining genomic stability and cellular functions, ensuring chromosomal integrity and cell viability. If the HRR pathway is impaired, double-stranded breaks are either not repaired, or repaired using the error-prone nonhomologous end joining (NHEJ) pathway. This results in genomic instability, which can lead to tumorigenesis.[6]

Mutations in the *BRCA1* and *BRCA2* genes, including small DNA variants and large gene rearrangements, are key drivers of HRD.[7,8] Aberrations that result in structural changes to chromosomes, or “genomic scars,” including loss of heterozygosity (LOH),[9] telomeric-allelic imbalance (TAI),[10] and large-scale state transitions (LST) are indicators of the inability to repair DNA damage.[11] These additional HRD biomarkers can be quantified and summed to generate a genomic instability score (GIS).

HRD in ovarian cancer

HRD is present in approximately 50% of high-grade serous ovarian cancer cases.[12] PARPi therapies such as LYNPARZA® exploit the impaired DNA repair mechanisms in HRD-positive tumors by blocking the repair of single-strand DNA breaks, leading to lethal DNA damage in cancer cells.[13] These therapies offer significant clinical benefits for patients with HRD-positive ovarian cancer.[14,15] Therefore, determining HRD status in tumors is critical for optimizing targeted therapies.

About TruSight Oncology Comprehensive HRD (DRAGEN)

TruSight Oncology Comprehensive HRD (DRAGEN) delivers a CE-marked IVD solution that enables clinical laboratories to identify HRD status in patients with ovarian cancer. The assay, powered by Illumina NGS technology and the Myriad Genetics GIS algorithm, detects single nucleotide variants (SNVs), insertions and deletions, and large rearrangements (exon-level deletions) in *BRCA1* and *BRCA2*. It assesses GIS by combining measures of LOH, TAI, and LST (Table 1).

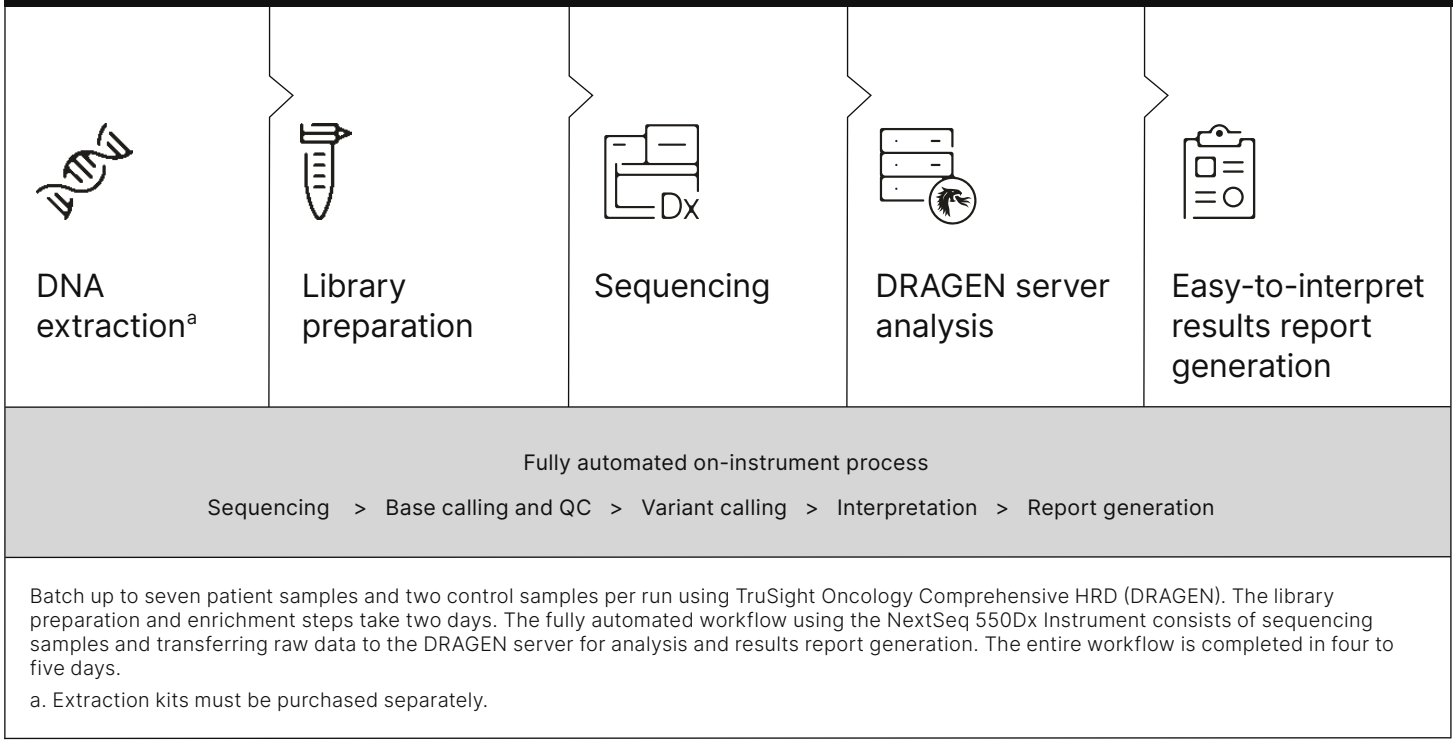
The kitted solution provides results through an integrated workflow (Figure 1) that includes library preparation, sequencing on the NextSeq™ 550Dx Instrument, and automated software pipelines powered by DRAGEN secondary analysis. This regulated HRD test enables laboratories to produce timely, accurate information on HRD status without the need to send out samples, supporting faster turnaround times.

Table 1: TruSight Oncology Comprehensive HRD (DRAGEN) at a glance

Feature	Description
Sequencing system	NextSeq 550Dx Instrument
Analysis[b]	Performed on the DRAGEN server
Patient sample throughput	6–7 patient samples/flow cell
Panel content	• *BRCA1* and *BRCA2* • GIS
Cross-ethnicity coverage	EAS, EUR, AFR, AMR, SAS
Variant types detected	• SNVs, insertions, deletions, and large rearrangements (exon-level deletions) in *BRCA1* and *BRCA2* • GIS, determined using a genome-wide SNP panel to assess genomic scars LOH, TAI, and LST
GIS	Numerical score
GIS algorithm	Powered by Myriad Genetics
DNA input requirement	40 ng DNA extracted from ovarian, fallopian tube, or primary peritoneal FFPE tissue
FFPE input requirement	Recommended tissue volume ≥ 1.0 mm^3 Minimum of 33% tumor content (by area) required to detect GIS
No. of biopsy slides	Minimum 5 recommended (10 µm sections, 20 mm^2 tissue area each)
Total assay time	4–5 days from nucleic acid to results report
Limit of blank (LoB)—false positives by variant type[a]	• *BRCA1* and *BRCA2* small DNA variants: 0% • *BRCA1* and *BRCA2* LRs: 0% • GIS: 0%
Limit of detection (LoD)[a]	• *BRCA1* and *BRCA2:* % VAF - SNVs: 5 - Insertions and deletions ≥ 10 bp: 6 - Insertions and deletions < 10 bp: 7 - Variants in homopolymer regions (≥ 5 bp): 7 - LRs < 3 exons: 61 - LRs ≥ 3 exons: 46 • GIS: 33% tumor content
Clinical performance characteristics[a]	• PPA: 97.6% (95% CI: 94.5%–99.2%) • NPA: 92.3% (95% CI: 86.9%–96.0%) • OPA: 95.3% (95% CI: 92.6%–97.3%)

a. Refer to product package insert for a full description of the study.
AFR, African; AMR, Admixed American; CI, confidence interval; EAS, East Asian; EUR, European; FFPE, formalin-fixed, paraffin-embedded; GIS, genomic instability score; LOH, loss of heterozygosity; LR, large rearrangement; LST, large-scale state transition; NPA, negative percent agreement; OPA, overall percent agreement; PPA, positive percent agreement; SAS, South Asian; SNP, single nucleotide polymorphism; SNV, single nucleotide variant; TAI, telomeric allelic imbalance; VAF, variant allele frequency.
b. For details on secondary and tertiary analysis, refer to the *Illumina Connected Run TruSight Oncology Comprehensive HRD (EU, DRAGEN) Analysis Module Workflow Guide (document # 200065740*).

Figure 1: TruSight Oncology Comprehensive HRD (DRAGEN) workflow



Batch up to seven patient samples and two control samples per run using TruSight Oncology Comprehensive HRD (DRAGEN). The library preparation and enrichment steps take two days. The fully automated workflow using the NextSeq 550Dx Instrument consists of sequencing samples and transferring raw data to the DRAGEN server for analysis and results report generation. The entire workflow is completed in four to five days.

a. Extraction kits must be purchased separately.

Companion diagnostic indication

TruSight Oncology Comprehensive HRD (DRAGEN) was developed as a companion diagnostic test (CDx) to identify ovarian cancer patients eligible for treatment with LYNPARZA® (Table 2). LYNPARZA® was approved in the European Union in 2020 as a first-line maintenance treatment with bevacizumab for patients with HRD-positive ovarian cancer.[16] The approval was based on a biomarker subgroup analysis of the PAOLA-1 Phase III clinical trial,[14] which showed that LYNPARZA®, in combination with bevacizumab maintenance treatment, demonstrated substantial improvement in progression-free survival versus bevacizumab alone for patients with HRD-positive ovarian cancer.

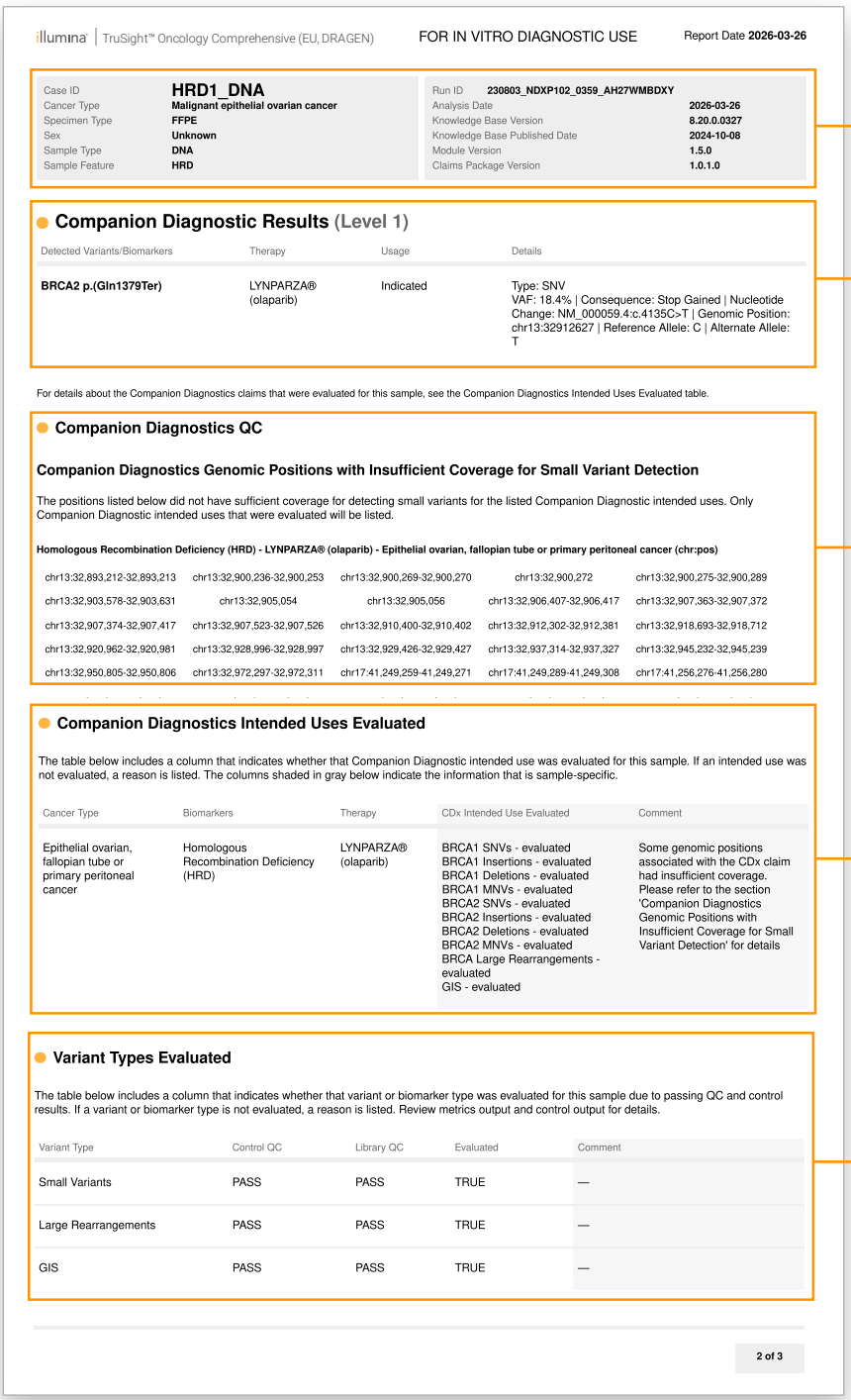
Table 2: CDx indication

Tumor type	Biomarker	Therapy
Ovarian cancer, including epithelial ovarian, fallopian tube, and primary peritoneal cancer	HRD (defined as deleterious or suspected deleterious mutations in *BRCA1* and *BRCA2* genes and/or positive GIS)	LYNPARZA® (olaparib)

One easy-to-interpret, actionable results report

TruSight Oncology Comprehensive HRD (DRAGEN) generates *BRCA1* and *BRCA2* variant data and GIS in a streamlined report (Figure 2). There is no need to search reports from multiple tests to identify significant variants.

Figure 2: Results report for TruSight Oncology Comprehensive HRD (DRAGEN)


illumina | TruSight™ Oncology Comprehensive (EU, DRAGEN) FOR IN VITRO DIAGNOSTIC USE Report Date 2026-03-26

Case ID HRD1_DNA
Cancer Type Malignant epithelial ovarian cancer
Specimen Type FFPE
Sex Unknown
Sample Type DNA
Sample Feature HRD
Run ID 230803_NDXP102_0359_AH27WMBDXY
Analysis Date 2026-03-26
Knowledge Base Version 8.20.0.0327
Knowledge Base Published Date 2024-10-08
Module Version 1.5.0
Claims Package Version 1.0.1.0

Companion Diagnostic Results (Level 1)

Detected Variants/Biomarkers	Therapy	Usage	Details
BRCA2 p.(Gln1379Ter)	LYNPARZA® (olaparib)	Indicated	Type: SNV VAF: 18.4% | Consequence: Stop Gained | Nucleotide Change: NM_000059.4:c.4135C>T | Genomic Position: chr13:32912627 | Reference Allele: C | Alternate Allele: T

For details about the Companion Diagnostics claims that were evaluated for this sample, see the Companion Diagnostics Intended Uses Evaluated table.

Companion Diagnostics QC

Companion Diagnostics Genomic Positions with Insufficient Coverage for Small Variant Detection

The positions listed below did not have sufficient coverage for detecting small variants for the listed Companion Diagnostic intended uses. Only Companion Diagnostic intended uses that were evaluated will be listed.

Homologous Recombination Deficiency (HRD) - LYNPARZA® (olaparib) - Epithelial ovarian, fallopian tube or primary peritoneal cancer (chr:pos)

chr13:32,893,212-32,893,213	chr13:32,900,236-32,900,253	chr13:32,900,269-32,900,270	chr13:32,900,272	chr13:32,900,275-32,900,289
chr13:32,903,578-32,903,631	chr13:32,905,054	chr13:32,905,056	chr13:32,906,407-32,906,417	chr13:32,907,363-32,907,372
chr13:32,907,374-32,907,417	chr13:32,907,523-32,907,526	chr13:32,910,400-32,910,402	chr13:32,912,302-32,912,381	chr13:32,918,693-32,918,712
chr13:32,920,962-32,920,981	chr13:32,928,996-32,928,997	chr13:32,929,426-32,929,427	chr13:32,937,314-32,937,327	chr13:32,945,232-32,945,239
chr13:32,950,805-32,950,806	chr13:32,972,297-32,972,311	chr17:41,249,259-41,249,271	chr17:41,249,289-41,249,308	chr17:41,256,276-41,256,280

Companion Diagnostics Intended Uses Evaluated

The table below includes a column that indicates whether that Companion Diagnostic intended use was evaluated for this sample. If an intended use was not evaluated, a reason is listed. The columns shaded in gray below indicate the information that is sample-specific.

Cancer Type	Biomarkers	Therapy	CDx Intended Use Evaluated	Comment
Epithelial ovarian, fallopian tube or primary peritoneal cancer	Homologous Recombination Deficiency (HRD)	LYNPARZA® (olaparib)	BRCA1 SNVs - evaluated BRCA1 Insertions - evaluated BRCA1 Deletions - evaluated BRCA1 MNVs - evaluated BRCA2 SNVs - evaluated BRCA2 Insertions - evaluated BRCA2 Deletions - evaluated BRCA2 MNVs - evaluated BRCA Large Rearrangements - evaluated GIS - evaluated	Some genomic positions associated with the CDx claim had insufficient coverage. Please refer to the section 'Companion Diagnostics Genomic Positions with Insufficient Coverage for Small Variant Detection' for details

Variant Types Evaluated

The table below includes a column that indicates whether that variant or biomarker type was evaluated for this sample due to passing QC and control results. If a variant or biomarker type is not evaluated, a reason is listed. Review metrics output and control output for details.

Variant Type	Control QC	Library QC	Evaluated	Comment
Small Variants	PASS	PASS	TRUE	—
Large Rearrangements	PASS	PASS	TRUE	—
GIS	PASS	PASS	TRUE	—

2 of 3

Patient sample information

Companion diagnostic results

Companion diagnostics QC

Companion diagnostics intended uses evaluated

Variant types evaluated

Validated solution

TruSight Oncology Comprehensive HRD (DRAGEN) is a validated DNA-to-results test that includes kitted reagents, a sequencing system, and analysis software. The test was developed using a rigorous design control process and validated across ~615 unique formalin-fixed, paraffin-embedded (FFPE) ovarian samples to ensure accurate, reproducible, and consistent data generation (Table 3).

Table 3: Validation studies using TruSight Oncology Comprehensive HRD (DRAGEN)	
Clinical bridging study for *BRCA1* and *BRCA2* variant detection and GIS using samples from the PAOLA-1 trial	Library stability
Accuracy	Limit of blank
Assay workflow guard banding	Limit of detection
Cross contamination/ carryover	Nucleic acid extraction kit evaluation
External control effectiveness	Kit shelf-life stability
Nucleic acid input titration guard banding	Reproducibility (including within-laboratory precision)
Interfering substances	Slide-mounted FFPE tissue stability
Kit in-use stability	Nucleic acid stability
Kit transport stability	

The clinical performance of the TruSight Oncology Comprehensive HRD (DRAGEN) as a CDx for LYNPARZA® was evaluated in a bridging study using samples from the PAOLA-1 trial, with the Myriad Genetics MyChoice® Plus test used as the clinical trial assay (CTA).[14] TruSight Oncology Comprehensive HRD (DRAGEN) showed high concordance with the CTA, achieving 95.3% overall agreement (Table 1 and Appendix), confirming its reliability in identifying HRD-positive patients eligible for LYNPARZA® therapy.

Using TruSight Oncology Comprehensive HRD (DRAGEN)

TruSight Oncology Comprehensive HRD (DRAGEN) provides a streamlined workflow that spans from sample input to the results report. After a two-day library prep protocol, samples are loaded onto a flow cell and into the sequencing system where the remainder of the test is fully automated, including sequencing, variant calling, interpretation, and reporting. The entire test, from nucleic acid extraction to results report, can be completed in four to five days.

Prepare libraries

TruSight Oncology Comprehensive HRD (DRAGEN) uses DNA extracted from FFPE tissue as input material. The gDNA is sheared and unique molecular identifiers (UMIs)[17] are added to the fragments. The UMIs enable detection of variants at low variant allele frequency (VAF) while simultaneously suppressing errors, providing high specificity. The tagged fragments are then subjected to targeted enrichment and amplification, generating sequence-ready libraries.

Enrich libraries to focus efforts

Library preparation is based on proven hybrid–capture chemistry using biotinylated probes and streptavidin-coated magnetic beads to purify selected targets from DNA-based libraries. Regions of interest hybridize to the biotinylated probes, are magnetically pulled down, and eluted to enrich the library pool.

Hybrid–capture chemistry offers several advantages over amplicon sequencing, including yielding data with fewer artifacts and dropouts and the ability to accommodate larger panel enrichment.

Sequence with diagnostic power

Prepared TruSight Oncology Comprehensive HRD (DRAGEN) libraries are sequenced on the CE-marked NextSeq 550Dx Instrument (Figure 3). This enables clinical laboratories to develop and perform NGS-based IVD assays. The NextSeq 550Dx Instrument features:

- A locked configuration with change control enabling laboratories to take advantage of current and future clinical testing options
- High-throughput capabilities to expand operations for larger, deeper studies or increase the number of patient samples run*
- Flexible analysis, including solid tumor profiling and microarray studies*

With prefilled reagent cartridges, starting a run on the NextSeq 550Dx Instrument is as easy as thaw, load, and go and takes roughly 30 minutes hands-on time. The intuitive interface enables efficient operation with minimal training and instrument set-up time. The NextSeq 550Dx Instrument can deliver > 90 Gb of high-quality data with over 75% of bases sequenced with a quality score of Q30 or higher in less than two days.[18]

Patient batching throughput

Using TruSight Oncology Comprehensive HRD (DRAGEN) with the NextSeq 550Dx Instrument, labs can batch up to seven patient samples with two controls per sequencing run and complete† the assay in 4–5 days.

Variant calling, interpretation, and reporting

All analysis for TruSight Oncology Comprehensive HRD (DRAGEN) is performed automatically on the NextSeq 550Dx Instrument using the DRAGEN Server and analysis module.

The TruSight Oncology Comprehensive HRD (DRAGEN) analysis module resides on the DRAGEN server paired with the NextSeq 550Dx Instrument to facilitate TruSight Oncology Comprehensive HRD (DRAGEN) run setup and to perform the secondary analysis of sequencing results. TruSight Oncology Comprehensive HRD (DRAGEN) analysis includes validation of run processing and quality control, followed by demultiplexing, FASTQ file generation, alignment, and variant calling:

- Demultiplexing separates data from pooled libraries based on the unique sequence indexes that were added during the library preparation procedure

Figure 3: The NextSeq 550Dx Instrument

Developed under design control and manufactured following good manufacturing practice (GMP) guidelines, the NextSeq 550Dx Instrument (in Dx mode) supports TruSight Oncology Comprehensive HRD (DRAGEN) workflow from sequencing through results report generation.

- FASTQ intermediate files contain the sequencing reads for each sample and quality scores, excluding reads from any clusters that did not pass the filter
- Sequencing reads are aligned against a reference genome to identify a relationship between the sequences and assigned a score based on regions of similarity; aligned reads are written to files in Binary Alignment Map (BAM) format

The analysis software module generates multiple intermediate files, including sequencing metrics and Variant Call Format (VCF) files. VCF files contain information about variants found at specific positions in a reference genome. Sequencing metrics and individual output files are generated for each sample. The TruSight Oncology Comprehensive HRD (DRAGEN) analysis module also performs CDx calling and results report generation. *BRCA1* and *BRCA2* variant data and GIS are summarized in the TruSight Oncology Comprehensive HRD (DRAGEN) results report.

* In research-use only (RUO) mode.
† Number of patient samples varies according to the number of controls run.

Reliable, high performance

The performance characteristics and reliability of TruSight Oncology Comprehensive HRD (DRAGEN) have been extensively tested to meet rigorous CE marking requirements (Table 3). Evaluations included limit of blank (LoB), limit of detection (LoD), and clinical performance (Appendix). Other validation studies included reproducibility and accuracy. Qualitative studies across multiple operators, instruments, reagent lots, and days showed high concordance with minimal variance. For detailed information on all validation studies performed, refer to the TruSight Oncology Comprehensive HRD (DRAGEN) package insert.

Bring HRD assessment into your lab

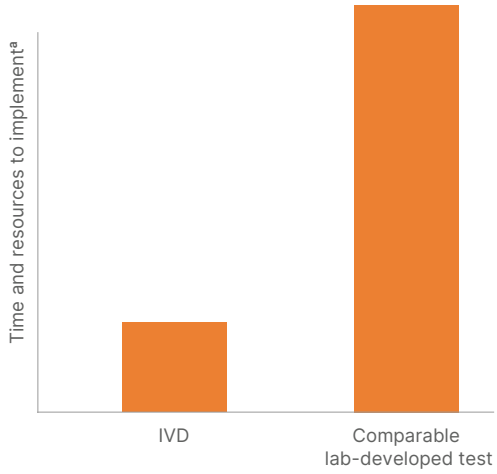
HRD assessment can inform therapy choices that have the potential to improve patient outcomes. HRD testing in your lab helps you:

- Be a precision medicine provider—Implement a state-of-the-art test and generate a clinically actionable report in 4–5 days with reduced quantity not sufficient (QNS) rates and improved test success rates
- Be a trusted partner—Consult with oncologists on therapy decisions and participate in molecular tumor boards

Implementing an in-house test can require significant time and effort. With the introduction of TruSight Oncology Comprehensive HRD (DRAGEN), Illumina has addressed some of the biggest challenges, streamlining the process. Starting with a validated, kitted solution:

- Reduces the time and expense of test implementation compared to a laboratory-developed test (LDT) (Figure 4)
- Expedites moving HRD to a routine test, closer to patient point of care
- Supports labs in achieving compliance with *In Vitro* Diagnostic Regulation (IVDR) requirements

Figure 4: Simpler, less burdensome implementation



TruSight Oncology Comprehensive HRD (DRAGEN) is a CE-marked *in vitro* diagnostic (IVD) that requires only ISO 15189 performance verification, which is less burdensome than the validation required for a test developed in the laboratory.

a. Illustrative example. Not meant to provide a precise comparison of time and resources.

Comprehensive support

A comprehensive support program is available to help labs expedite implementation and certification to ensure a smooth integration. The program provides:

- Onboarding plan to expedite test verification
- Laboratory training, including wet-lab instruction and run assessment, with the expert Illumina Field Application Specialist team
- Verification protocol
- Training certification
- 24/5 technical support
- Ongoing support from the Illumina Medical Affairs team for medical inquiries

Access to reimbursement

Test coverage is an important consideration when planning to establish in-house testing. Illumina has established a dedicated Market Access team that is actively working with payers to expand HRD test reimbursement. Discuss available coverage options with your local Illumina Account Manager.

Summary

Assessing HRD as a biomarker in ovarian cancer can improve patient outcomes by informing therapy selection. TruSight Oncology Comprehensive HRD (DRAGEN) enables clinical laboratories to perform in-house HRD testing with a streamlined workflow, quality-controlled reagents, and automated clinical software. This validated, CE-marked solution delivers results within 4–5 days. The clear, clinically relevant results report accurately categorizes ovarian tumors as HRD positive or negative to support evidence-based decisions for therapy selection.

Learn more →

TruSight Oncology Comprehensive HRD (DRAGEN)

NextSeq 550Dx Instrument

HRD Detection in Cancer

Ordering information

Product	Catalog no.
TruSight Oncology Comprehensive DRAGEN Kit	20140799
TruSight Oncology Comprehensive HRD (DRAGEN)	20134650
TruSight Oncology DNA Control v2	20090155
NextSeq 550Dx Instrument	20005715
DRAGEN IVD Server	20086130
NextSeq 550Dx High-Output Reagent Kit v2.5 (300 cycles)[a]	20028871

a. Class I sequencing consumables have single lot shipment, kit lot testing, advance change notification, and a Certificate of Analysis available for each lot. Reagents are developed under design control principles, manufactured under current good manufacturing practices (cGMP), and verified to ensure specification compliance.

Appendix

Results are presented for TruSight Oncology Comprehensive HRD (DRAGEN) for the following studies:

- Limit of blank (LoB) study
- Limit of detection (LoD) study
- Clinical performance characteristics

For a description of all performance characteristics, refer to the TruSight Oncology Comprehensive HRD (DRAGEN) package insert.

Limit of blank (LoB) study

The percentage of false positives (out of the total expected negatives) was assessed through an LoB study by replicate testing of FFPE benign samples from adjacent ovarian tissue that should be free of deleterious *BRCA1* and *BRCA2* variants (small DNA variants and large rearrangements) and be GIS negative.

False positives by variant type

Variant type	False positives (n/N)
BRCA1/2 small DNA variants	0% (0/3,076,657)
BRCA1/2 large rearrangements	0% (0/384)
GIS	0% (0/192)

GIS, genomic instability score.

Limit of detection (LoD) study

The LoD of deleterious *BRCA1* and *BRCA2* small DNA variants (SNVs, insertions and deletions ≥ 10 bp, insertions and deletions < 10 bp, variants in homopolymer regions ≥ 5 bp), *BRCA1* and *BRCA2* large rearrangements (< 3 exons and ≥ 3 exons), and GIS were determined in DNA isolated from ovarian cancer FFPE samples. The LoD for GIS was defined as the lowest tumor content that achieves ≥ 95% GIS detection. Ovarian cancer FFPE samples were used in the detection of *BRCA1* and *BRCA2* small DNA variants, *BRCA1* and *BRCA2* large rearrangements ≥ 3 exons, and GIS. A breast cancer FFPE sample was used for detecting *BRCA1* and *BRCA2* large rearrangements < 3 exons, due to unavailability of ovarian cancer FFPE samples.

LoD for *BRCA1/2* small DNA variants, *BRCA1/2* LR, and GIS

Variant type	Variant class	C95 (% VAF)
BRCA1/2 small DNA variants	SNVs	5
	Insertions and deletions ≥ 10 bp	6
	Insertions and deletions < 10 bp	7
	Variants in homopolymer regions (≥ 5bp)	7
BRCA1/2 large rearrangement	< 3 exons	61
	≥ 3 exons	46
GIS	GIS	33% tumor content

C95, 95% detection concentration threshold; GIS, genomic instability score; SNV, single nucleotide variant; VAF, variant allele frequency.

Clinical performance characteristics

The clinical performance of the TruSight Oncology Comprehensive HRD (DRAGEN) assay for detecting *BRCA1* and *BRCA2* variants (small DNA variants and large rearrangements) and GIS in patients with ovarian cancer who may benefit from treatment with LYNPARZA® was demonstrated in a clinical bridging study. Residual tumor FFPE samples from patients enrolled in the PAOLA-1 clinical trial[14] were retrospectively tested with TruSight Oncology Comprehensive HRD (DRAGEN) and the results compared with the CTA. TruSight Oncology Comprehensive HRD (DRAGEN) showed high concordance with the CTA, achieving 95.3% overall agreement, confirming its reliability in identifying HRD-positive patients eligible for LYNPARZA® therapy.

Concordance between TruSight Oncology Comprehensive HRD (DRAGEN) and CTA for detection of HRD

		CTA result		
		HRD positive	HRD negative	All
TruSight Oncology Comprehensive HRD (DRAGEN) result	HRD positive	204	12	216
	HRD negative	5	144	149
	All	209	156	365
Agreement[a]	PPA	97.6 (95% CI: 94.5%–99.2%)		
	NPA	92.3 (95% CI: 86.9%–96.0%)		
	OPA	95.3 (95% CI: 92.6%–97.3%)		

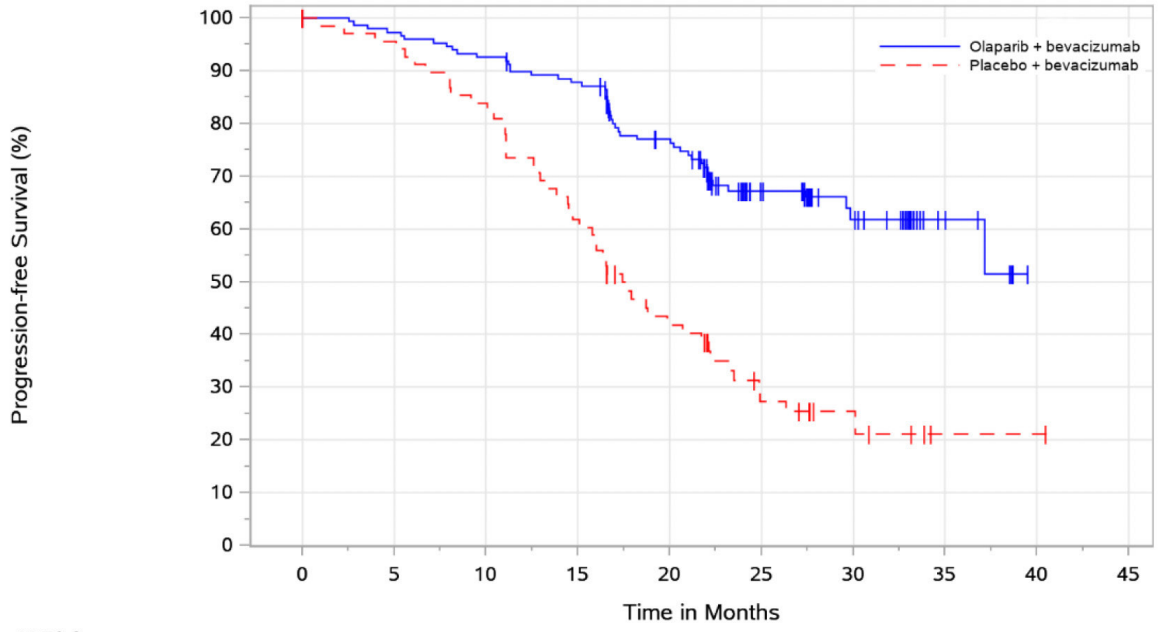
a. 95% two-sided CI calculated via the Wilson Score method.

CI, confidence interval; CTA, clinical trial assay; HRD, homologous recombination deficiency; NPA, negative percent agreement; OPA, overall percent agreement, PPA, positive percent agreement.

Clinical efficacy results

In CTA and TSO Comprehensive HRD (DRAGEN) HRD-positive populations, the progression-free survival (PFS) hazard ratio was 0.33 (95% CI: 0.25, 0.45) and 0.32 (95% CI: 0.22, 0.48), respectively, and represented a 67% and 68% reduction in the risk of progression or death for participants in the LYNPARZA® plus bevacizumab group compared to the placebo plus bevacizumab group. A sensitivity analysis addressing the efficacy of imputed missing CDx results demonstrated that the PFS hazard ratios in the imputed HRD-positive populations were consistent with the primary analysis estimates.

Kaplan-Meier Curve - PFS in HRD-positive participants identified by TSO Comprehensive HRD (DRAGEN)



At Risk

Olaparib + bevacizumab	149	144	137	129	101	60	29	8	0	0
Placebo + bevacizumab	71	65	57	42	26	14	6	1	1	0

References

1. Denny JC, Collins FS. Precision medicine in 2030-seven ways to transform healthcare. *Cell.* 2021;184(6):1415-1419. doi:10.1016/j.cell.2021.01.015
2. Wheler JJ, Janku F, Naing A, et al. Cancer therapy directed by comprehensive genomic profiling: a single center study. *Cancer Res.* 2016;76(13):3690-3701. doi:10.1158/0008-5472.CAN-15-3043
3. Wagener-Ryczek S, Merkelbach-Bruse S, Siemanowski J. Biomarkers for homologous recombination deficiency in cancer. *J Pers Med.* 2021;11(7):612. doi:10.3390/jpm1107061
4. Ledermann JA, Drew Y, Kristeleit RS. Homologous recombination deficiency and ovarian cancer. *Eur J Cancer.* 2016;60:49-58. doi:10.1016/j.ejca.2016.03.005
5. Yamamoto H, Hirasawa A. Homologous recombination deficiencies and hereditary tumors. *Int J Mol Sci.* 2021;23(1):348. doi:10.3390/ijms23010348
6. O'Connor MJ. Targeting the DNA damage response in cancer. *Mol Cell.* 2015;60(4):547-560. doi:10.1016/j.molcel.2015.10.040
7. Prakash R, Zhang Y, Feng W, Jasin M. Homologous recombination and human health: the roles of *BRCA1*, *BRCA2*, and associated proteins. *Cold Spring Harb Perspect Biol.* 2015;7(4):a016600. doi:10.1101/cshperspect.a016600
8. King MC. "The race" to clone *BRCA1*. *Science.* 2014;343(6178):1462-1465. doi:10.1126/science.1251900
9. Abkevich V, Timms KM, Hennessy BT, et al. Patterns of genomic loss of heterozygosity predict homologous recombination repair defects in epithelial ovarian cancer. *Br J Cancer.* 2012;107(10):1776-1782. doi:10.1038/bjc.2012.451
10. Birkbak NJ, Wang ZC, Kim JY, et al. Telomeric allelic imbalance indicates defective DNA repair and sensitivity to DNA-damaging agents. *Cancer Discov.* 2012;2(4):366-375. doi:10.1158/2159-8290.CD-11-0206
11. Popova T, Manié E, Rieunier G, et al. Ploidy and large-scale genomic instability consistently identify basal-like breast carcinomas with *BRCA1/2* inactivation. *Cancer Res.* 2012;72(21):5454-5462. doi:10.1158/0008-5472.CAN-12-1470
12. Quesada S, Fabbro M, Solassol J. Toward more comprehensive homologous recombination deficiency assays in ovarian cancer, Part 1: Technical considerations. *Cancers (Basel).* 2022;14(5):1132. doi:10.3390/cancers14051132
13. Farmer H, McCabe N, Lord CJ, et al. Targeting the DNA repair defect in *BRCA* mutant cells as a therapeutic strategy. *Nature.* 2005;434(7035):917-921. doi:10.1038/nature03445
14. Ray-Coquard I, Pautier P, Pignata S, et al. LYNPARZA® plus bevacizumab as first-line maintenance in ovarian cancer. *N Engl J Med.* 2019;381(25):2416-2428. doi:10.1056/NEJMoa1911361
15. Carballo EV, Kim KH, Penn CA. Trends in estimated PARP inhibitor eligibility and benefit among US epithelial ovarian cancer patients. *Gynecol Oncol.* 2024;187:204-211. doi:10.1016/j.ygyno.2024.05.014
16. AstraZeneca. Lynparza® approved in the EU as 1st-line maintenance treatment with bevacizumab for HRD-positive advanced ovarian cancer. astrazeneca.com/media-centre/press-releases/2020/lynparza-approved-in-the-eu-for-wider-ovarian-use.html#. Published November 5, 2020. Accessed March 27, 2026.
17. Illumina. TruSight Oncology UMI Reagents technical note. illumina.com/content/dam/illumina-marketing/documents/products/datasheets/trusight-oncology-umi-reagents-datasheet-1000000050425.pdf. Published 2018. Accessed March 27, 2026.
18. Illumina. NextSeq 550Dx Instrument. illumina.com/content/dam/illumina/gcs/assembled-assets/marketing-literature/nextseq-550-dx-spec-sheet-m-gl-00035/nextseq-550-dx-instrument-spec-sheet-m-gl-00035.pdf. Published 2025. Accessed March 27, 2026.

Intended use statement

TruSight™ Oncology Comprehensive HRD (DRAGEN™) is a qualitative *in vitro* diagnostic test that uses targeted next-generation sequencing to enable assessment of Homologous Recombination Deficiency (HRD) using DNA extracted from formalin-fixed, paraffin-embedded (FFPE) tumor tissue samples from ovarian cancer patients using the Illumina® NextSeq™ 550Dx Instrument. The test can be used to detect single nucleotide variants, insertions, deletions, and large rearrangements in *BRCA1* and *BRCA2* genes, and report a Genomic Instability Score (GIS).

The test is intended to be used as a companion diagnostic to identify cancer patients who may benefit from treatment with the targeted therapy listed in Table 4, in accordance with the approved therapeutic product labeling.

Table 4: Companion diagnostic indication

Tumor type	Biomarker	Therapy
Ovarian cancer, including epithelial ovarian, fallopian tube, and primary peritoneal cancer	Homologous Recombination Deficiency (HRD) (defined as deleterious or suspected deleterious mutations in *BRCA1* and *BRCA2* genes and/or positive Genomic Instability Score)	LYNPARZA® (olaparib)

illumina®

1.800.809.4566 toll-free (US) | +1.858.202.4566 tel
techsupport@illumina.com | www.illumina.com

M-EMEA-01635 v2.0