Next-generation sequencing

Future clinical perspective of HRD testing in ovarian cancer samples using NGS CGP

Summary of GenomeWeb™ webinar, May 23, 2023, presented by Dr. Nicola Normanno, Director, Translational Research, National Cancer Institute Pascale Foundation, Italy

Performance of HRD testing with the Ion Torrent™ Oncomine™ Comprehensive Assay Plus

- Retrospective multicenter study with n = 100 stage III–IV ovarian cancer samples treated with chemotherapy from the MITO-16/MaNGO-OV2 clinical study.
- Both the causes (*BRCA1/BRCA2* pathogenic mutations) and consequences of genomic scarring through the genomic instability metric (GIM) were measured to assess for homologous recombination deficiency (HRD) using the Oncomine Comprehensive Assay Plus.
- GIM is a value between 0 and 100 that summarizes the unbalanced copy number changes in autosomes, with a threshold set at GIM ≥16 to determine GIM-high status in ovarian cancer samples.
- The Oncomine Comprehensive Assay Plus had acceptable overall concordance with the reference method at 3 levels: *BRCA1/BRCA2* mutational status, genomic instability (GI) using GIM, and HRD status.
- HRD assessment with the Oncomine Comprehensive Assay Plus was part of a clinical research study comparing retrospective, de-identified clinical data, and trends similar to those of the reference method were demonstrated.

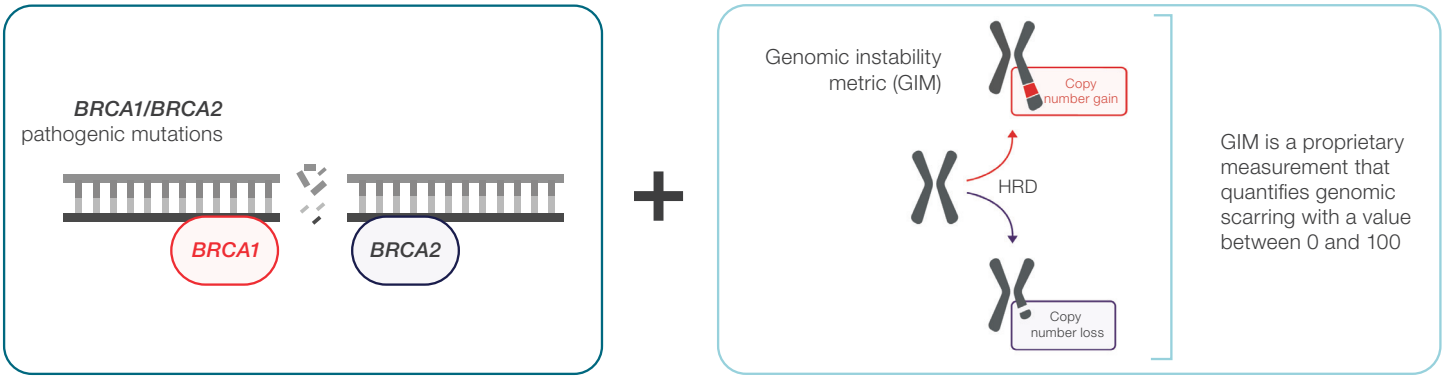

Figure 1. The Oncomine Comprehensive Assay Plus measures the causes and consequences of HRD in ovarian cancer.

BRCA1/2 mutational status(+) and GIM(–) = HRD(+)

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BRCA1/2 mutational status(–) and GIM(+) = HRD(+)

BRCA1/2 mutational status(–) and GIM(–) = HRD(–)

Figure 2. HRD status is determined from *BRCA1/BRCA2* mutational status and GIM.

Table 1. *BRCA1/BRCA2* mutational status using the Oncomine Comprehensive Assay Plus.

		Reference method		
		Positive	Negative	Total
Oncomine Comprehensive Assay Plus	Positive	28	1	29
	Negative	3*	59	62
	Total	31	60	91

***BRCA1/BRCA2* status:** Oncomine Comprehensive Assay Plus vs. reference method	
Sensitivity	90.3%
Specificity	98.3%
Overall concordance	95.6%

* *BRCA1* variants detected by the Oncomine Comprehensive Assay Plus but not classified as clinically significant.

Table 2. GI status using the Oncomine Comprehensive Assay Plus.

		Reference method		
		Positive	Negative	Total
Oncomine Comprehensive Assay Plus	Positive	47	8	55
	Negative	2	28	30
	Total	49	36	85

GI status: Oncomine Comprehensive Assay Plus vs. reference method	
Sensitivity	95.9%
Specificity	77.8%
Overall concordance	88.2%

Table 3. HRD status (combined) using the Oncomine Comprehensive Assay Plus.

		Reference method		
		Positive	Negative	Total
Oncomine Comprehensive Assay Plus	Positive	51	7	58
	Negative	1	27	28
	Total	52	34	86

HRD status (combined): Oncomine Comprehensive Assay Plus vs. reference method	
Sensitivity	98.1%
Specificity	79.4%
Overall concordance	90.7%

Table 4. HRD status assessment with the Oncomine Comprehensive Assay Plus demonstrated similar mathematical trends (RR, PFS, OS) relative to the reference method in this clinical research study.

	Reference method		Oncomine Comprehensive Assay Plus	
	HRD+	HRD–	HRD+	HRD–
RR*	82.4%	60.0%	78.4%	60.0%
Median PFS* (months)	18.6%	20.2%	19.8%	16.3%
Median OS* (months)	40.6%	41.1%	41.2%	29.7%

* RR: response rate; PFS: progression-free survival; OS: overall survival.

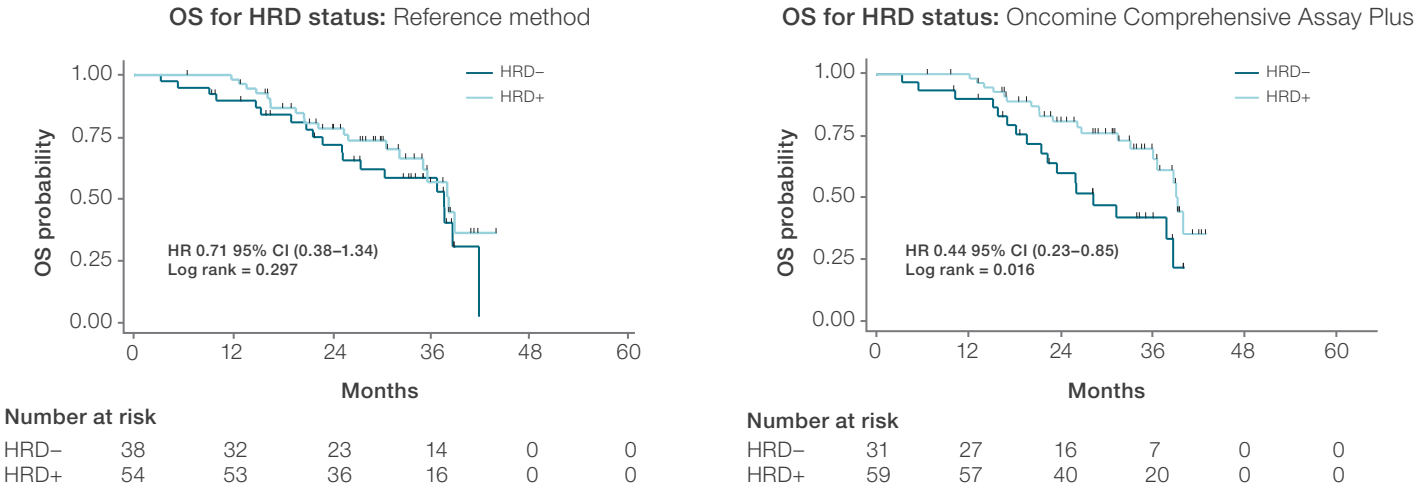

Figure 3. HRD assessment with the Oncomine Comprehensive Assay Plus demonstrated similar mathematical trends (OS) relative to the reference method in this clinical research study.

Table 5. HRD status assessment with the Oncomine Comprehensive Assay Plus demonstrated similar mathematical trends (PFS univariate, PFS multivariate) relative to the reference method in this clinical research study.

	PFS univariate		PFS multivariate*	
	HR	*P*-value	HR	*P*-value
Reference test (HRD+ vs. HRD–)	0.68	0.101	0.53	0.010
Oncomine Comprehensive Assay Plus (HRD+ vs. HRD–)	0.65	0.090	0.46	0.006

* Each multivariate model was adjusted for age, performance status, residual disease, and International Federation of Gynecology and Obstetrics (FIGO) stage.

Conclusions

- Based on this study, the Oncomine Comprehensive Assay Plus is suitable for detecting HRD as a complex genomic signature, within its offering as a comprehensive genomic profiling (CGP) assay.
- The Oncomine Comprehensive Assay Plus had a good HRD concordance to the reference method with 98.1% sensitivity, 79.4% specificity, and 90.7% overall concordance.
- HRD status assessment with the Oncomine Comprehensive Assay Plus in this clinical research study demonstrated similar mathematical trends relative to the reference method; this will need to be investigated further in future research studies.
- The Oncomine Comprehensive Assay Plus is for research use only, and this analysis was performed as part of a retrospective clinical research study. No patient management decisions were made based on these results.

Learn more about the Oncomine Comprehensive Assay Plus and watch the webinar at **thermofisher.com/oncomine-ocaplus**