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Validation study of the "NOGGO-GIS ASSAY" based on ovarian cancer samples from the first-line PAOLA-1/ENGOT-ov25 phase-III trial

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NOGGO e.V. Forschung – Fortbildung – Fortschritt

Declaration of interests

- I declare that I have no conflicts of interests
- This study was partially funded by Agilent
- I have advisory roles for

  Agilent, Novartis, Boehringer, MSD, Bayer, Lilly, Astra Zeneca

Assay requirements

NOGGO GIS Assay V1

- genomic instability / HRD
- part of modular wet-lab and bioinformatics workflow with adjustable content
- BRCA1 and BRCA2 mutations including large deletions
- covers all exons of HRR Genes (RAD51, PALB etc.)
- reliable detection of LOH for tumour suppressor genes
- detection of therapeutically relevant driver mutations for HRD negative patients
  - HER2 amp, KRAS, BRAF, PIK3CA, EGFR etc.
- reliable detection on minimum of 40ng of DNA from a single FFPE tumour sample
- robust chemistry with low failure rate

NOGGO GIS Assay V1

57 genes, approx. 20.000 SNP loci and a total size of 2.9Mb

ABRAXAS1	BRIP*	FANCC*	MRE11A*	RAD51B*
APC	BUB1B	FANCD2*	MSH2	RAD51C*
AR	CDH1	FANCE*	MSH6	RAD51D*
ARID1A*	CDK12*	FANCF*	NBN*	RAD52*
ATM*	CHEK1*	FANCG	**NRAS**	RAD54L*
ATR*	CHEK2*	FANCI*	PALB2*	RPA1*
ATRX	CTNNB1	FANCL*	**PIK3CA**	STK11
BARD1*	**EGFR**	FANCM*	PMS2	TP53
BLM*	EMSY*	HDAC2*	PPP2A2R	XRCC2*
BRAF	**ERBB2**	HOXB3	PTEN	
BRCA1*	ESR1	**KRAS**	RAD50*	
BRCA2*	FANCA*	MLH1*	RAD51*	

*HRR-Genes; Bold: tumor driver genes

- Covers BRCA1/BRCA2 and ~ 30 genes associated to HRR pathway plus some typical cancer associated genes (3x enrichment)
- Covers > 20.000 SNP positions for genomic instability status (Agilent CNV backbone, 1x enrichment)

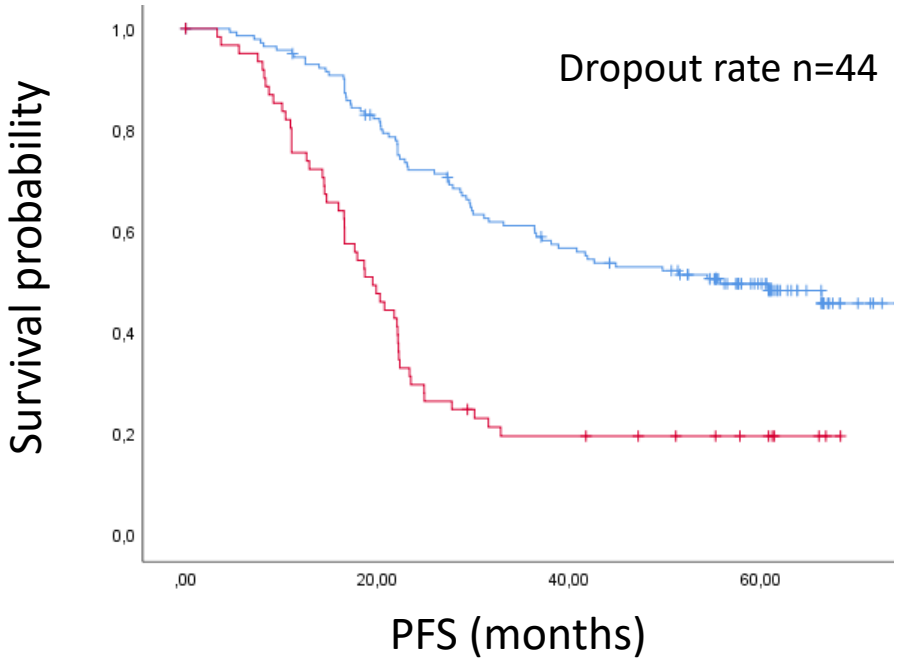
Assay specifications for GIS module

Agilent XT HS2 chemistry and open source bioinformatics

- based on Agilent 20.000 SNP back bone
- minimum 40ng of FFPE DNA input
- 20 million read pairs (2x 80bp) on Illumina platform
- automated on Agilent Bravo, Magnis and Hamilton liquid handlers
- turn around time 10 days
- PureCN and open access software on GIT HUB
- integrated software solution will be available from Agilent

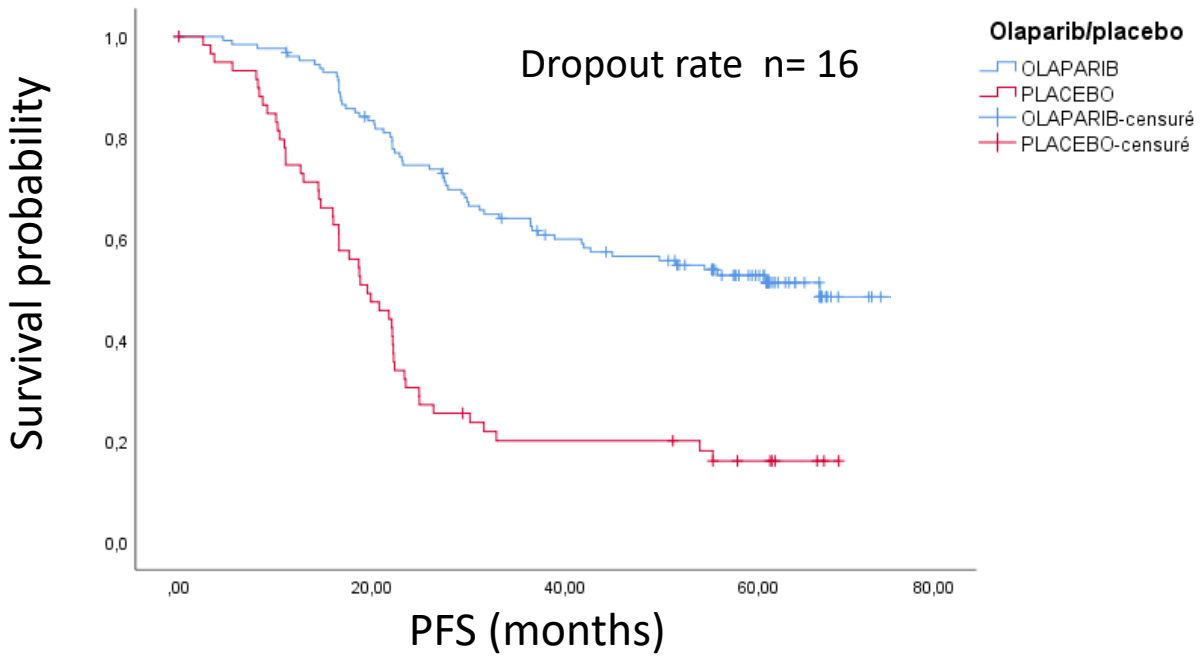
PFS HRD+ (Olaparib+Bev. vs. Bev.)

PAOLA1 trial assay



p-value	HR	95,0% CI for HR		n
0.000	**0.352**	0.243	0.510	383

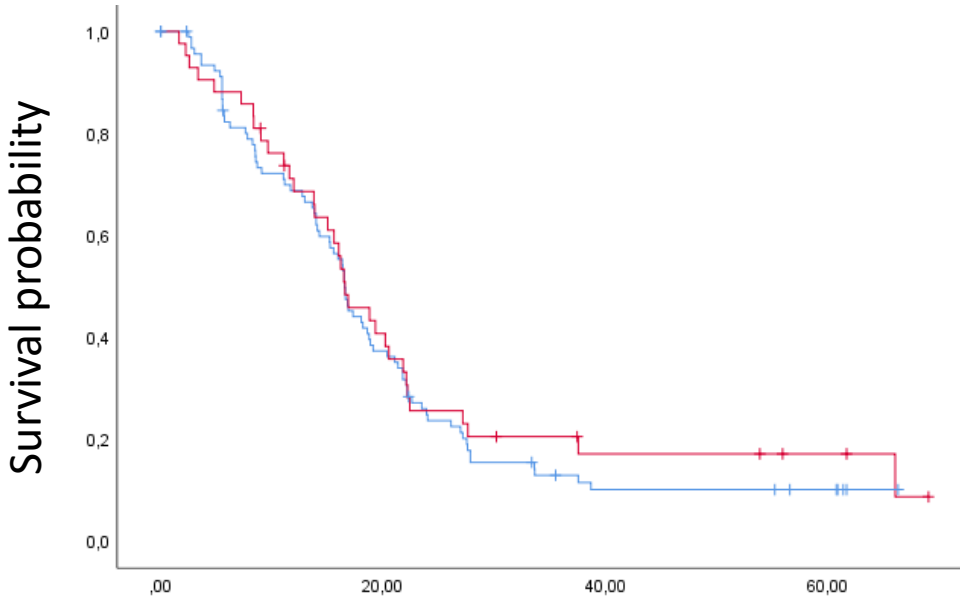
NOGGO GIS Assay V1



p-value	HR	95,0% CI for HR		n
0.000	**0.310**	0.211	0.456	383

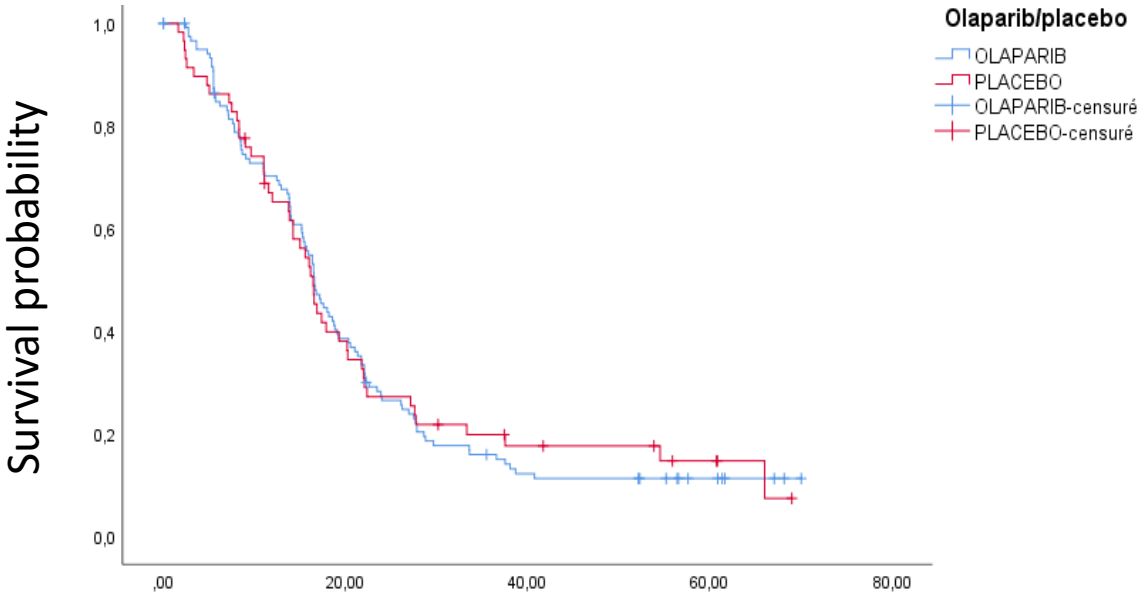
PFS HRD- (Olaparib+Bev. vs. Bev.)

PAOLA1 trial assay



p-value	HR	95,0% CI for HR		n
0.560	**1.128**	0.753	1.688	383

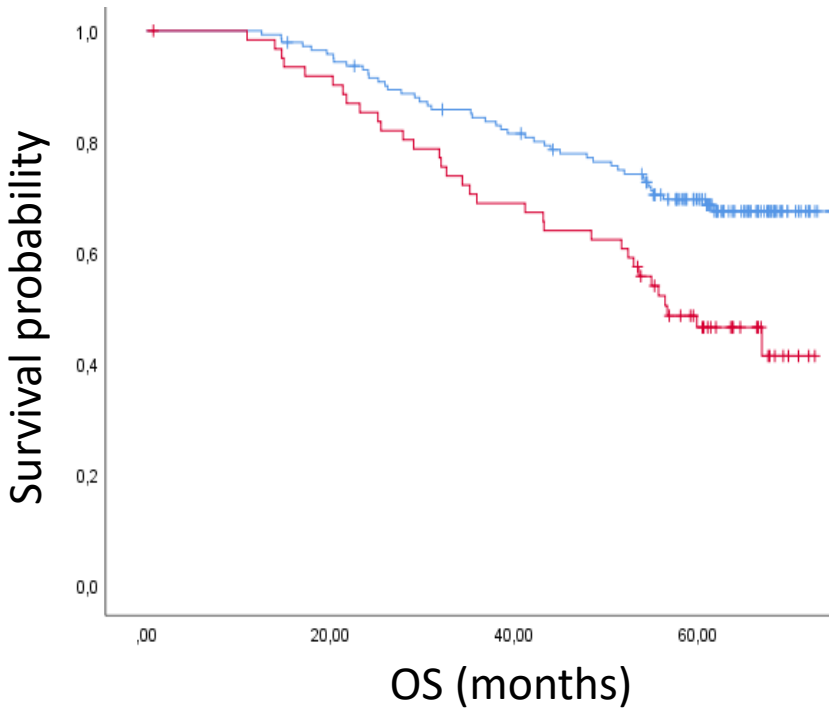
NOGGO GIS Assay V1



p-value	HR	95,0% CI for HR		n
0.897	**1.023**	0.726	1.441	383

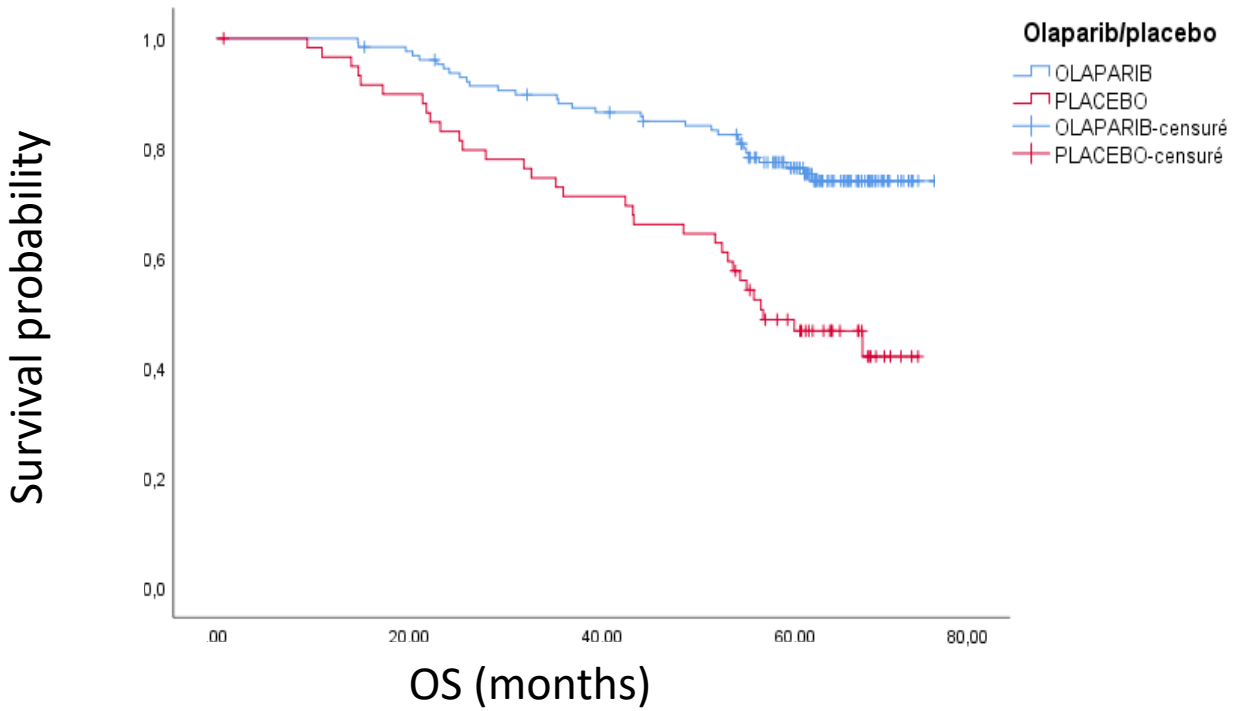
OS HRD+ (Olaparib+Bev. vs. Bev.)

PAOLA1 trial assay



p-value	HR	95,0% CI for HR		n
0.003	**0.500**	0.318	0.786	383

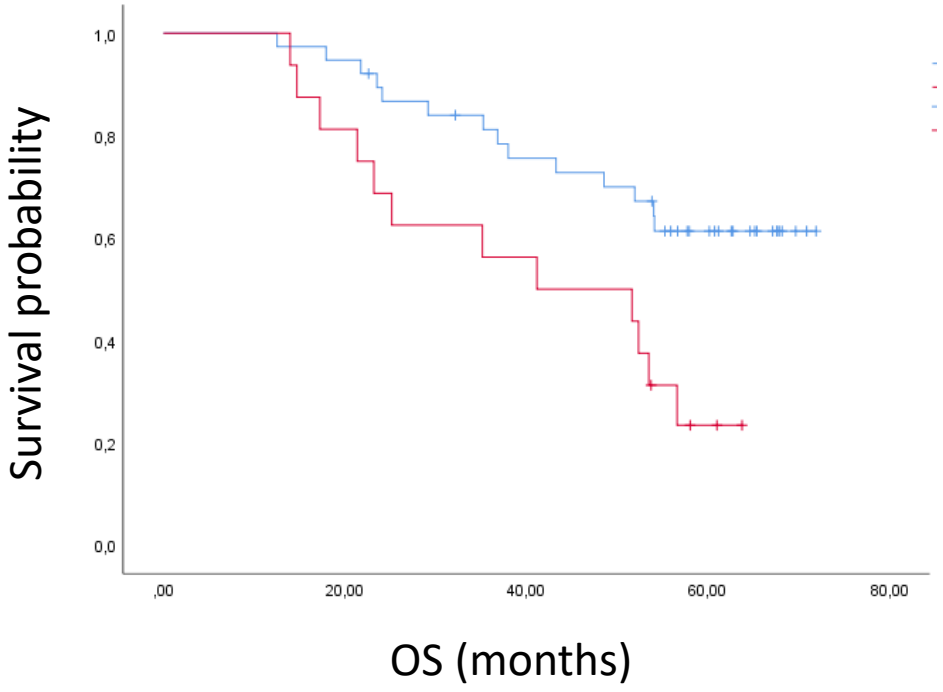
NOGGO GIS Assay V1



p-value	HR	95,0% CI for HR		n
0.000	**0.370**	0.226	0.607	383

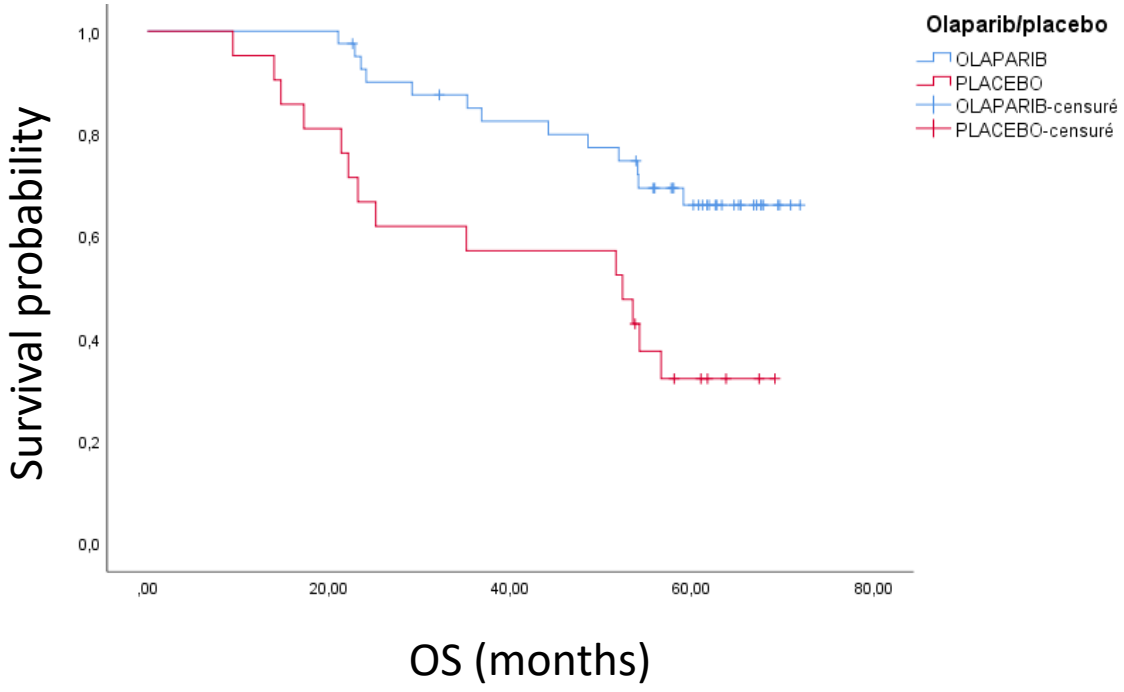
OS HRD+ subgroup **BRCA wild type** (Olaparib+Bev. vs. Bev.)

PAOLA1 trial assay



p-value	HR	95,0% CI for HR		n
0.011	**0.364**	0.167	0.790	54

NOGGO GIS Assay V1



p-value	HR	95,0% CI for HR		n
0.006	**0.346**	0.162	0.738	62

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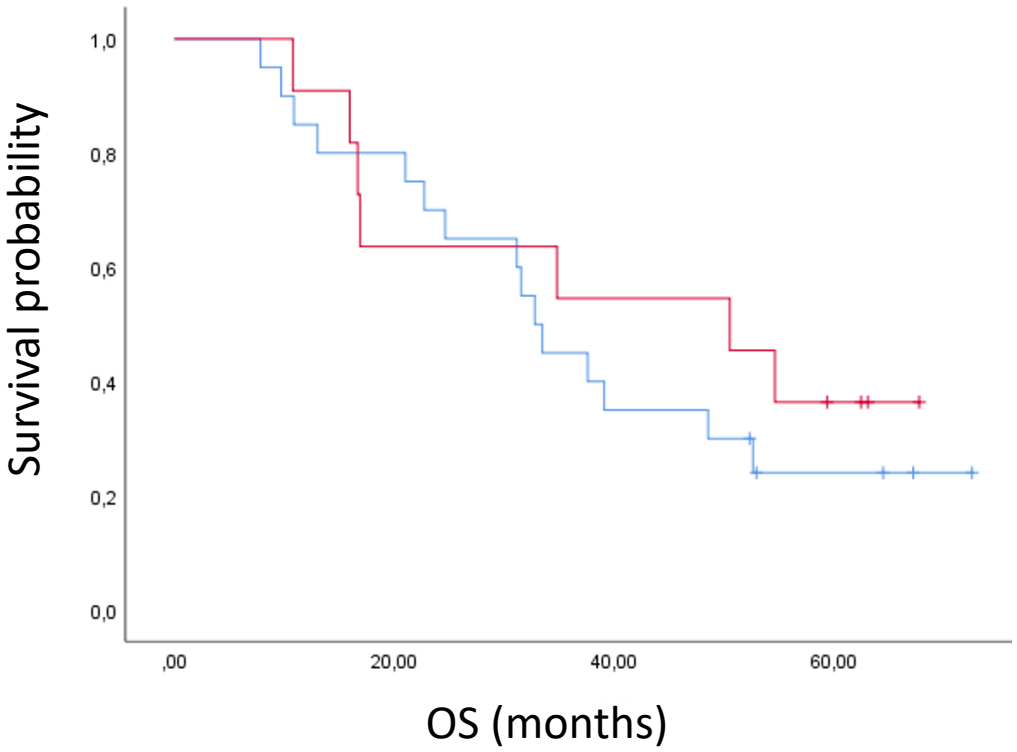
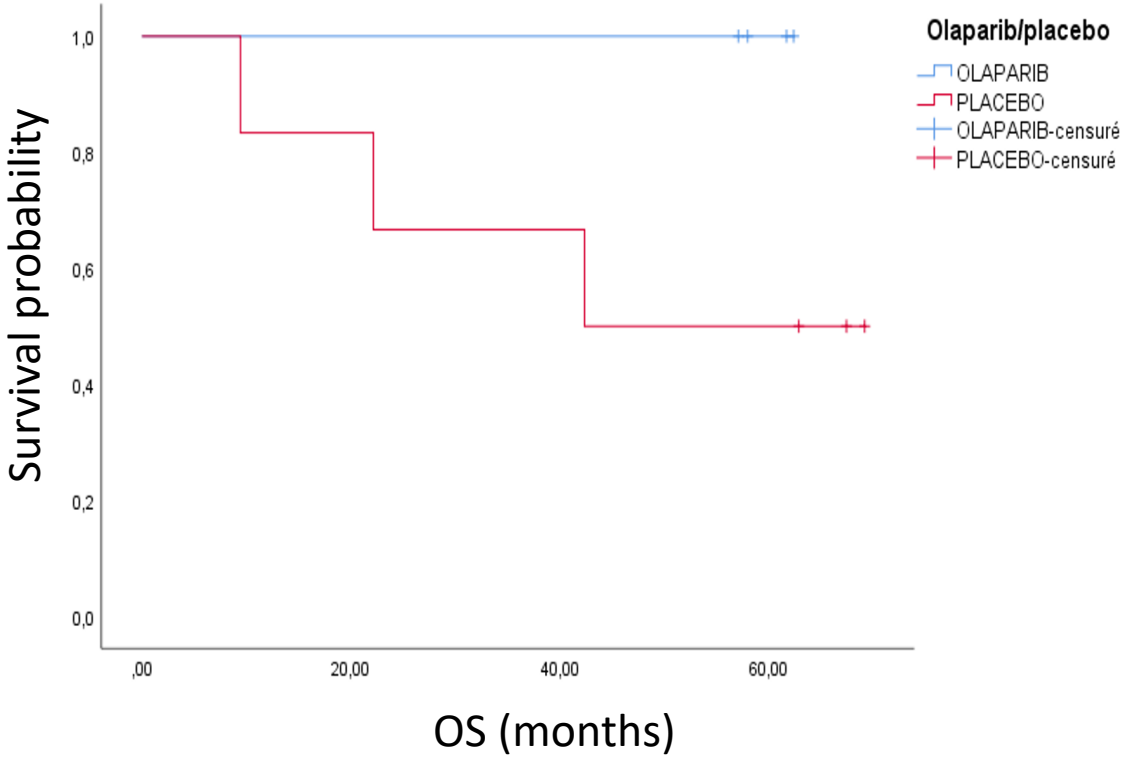
OS for patients with unknown HRD status n=44

NOGGO GIS Assay V1 results of trial assay drop out cases

NOGGO HRD-



NOGGO HRD+



NOGGO GIS V1 assay Summary

- low failure rate due to low DNA input and bioinformatics (44 vs 16)
- based on robust Agilent HS2 Hybrid Capture NGS chemistry with Illumina sequencing
- GIS determination only requires SNP backbone
- similar PFS and OS data compared to Myriad MyChoice DX
- based on PureCN and software made available on GIT HUB
- sample processing at HP-Hamburg or locally as LDT
- full implementation will be offered by Agilent

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Thank you for your attention

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ARCAGY - GINECO

CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN

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European Network of Gynaecological Oncological Trial groups