GeparOLA - GBG 90

Neoadjuvant paclitaxel/olaparib in comparison to paclitaxel/carboplatinum in patients with HER2-negative early breast cancer and homologous recombination deficiency – long-term survival of the GeparOLA study

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-This is a joint study by GBG and AGO-B-

Background

- The randomized phase II GeparOLA study investigated the neoadjuvant treatments
  - olaparib plus paclitaxel (PO) followed by EC and
  - carboplatinum plus paclitaxel (PCb) followed by EC

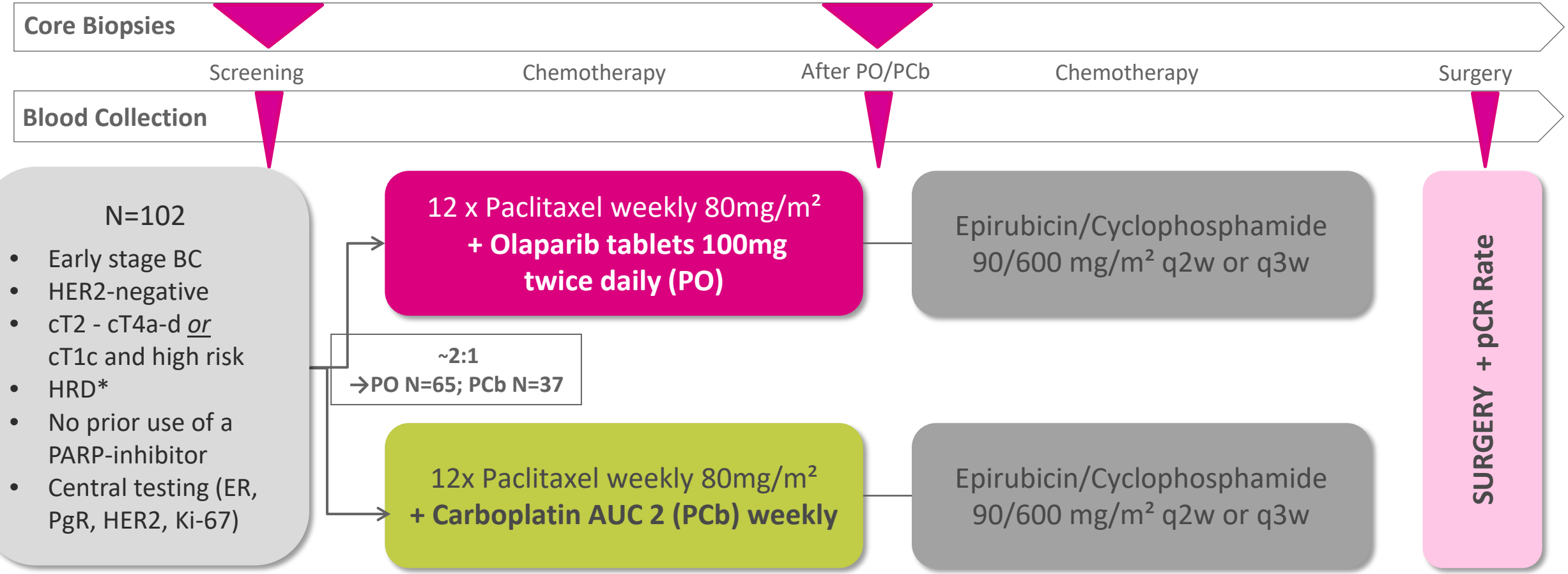
  in early BC patients with HER2-negative homologous recombination deficient (HRD) tumors.

- The pCR Rate in the PO arm was 55.1% and 48.6% in the PCb arm.
- Olaparib was significantly better tolerated than carboplatinum.

- Here, we report long-term survival data with a median FU of 49.8 months.

Fasching et *al*. Ann Oncol. 2020

GeparOla Study Design



Stratification Factors:

- Age (<40 years vs >= 40 years)
- Hormone Receptor Status (HR+ vs HR-)

* Patients with either a known somatic or germline *BRCA*1/2 mutation or HRD score[1] high (defined as a MyChoice™ Score of ≥42)

Fasching et *al*. Ann Oncol. 2020
[1]Timms et al. Breast Cancer Res 2014

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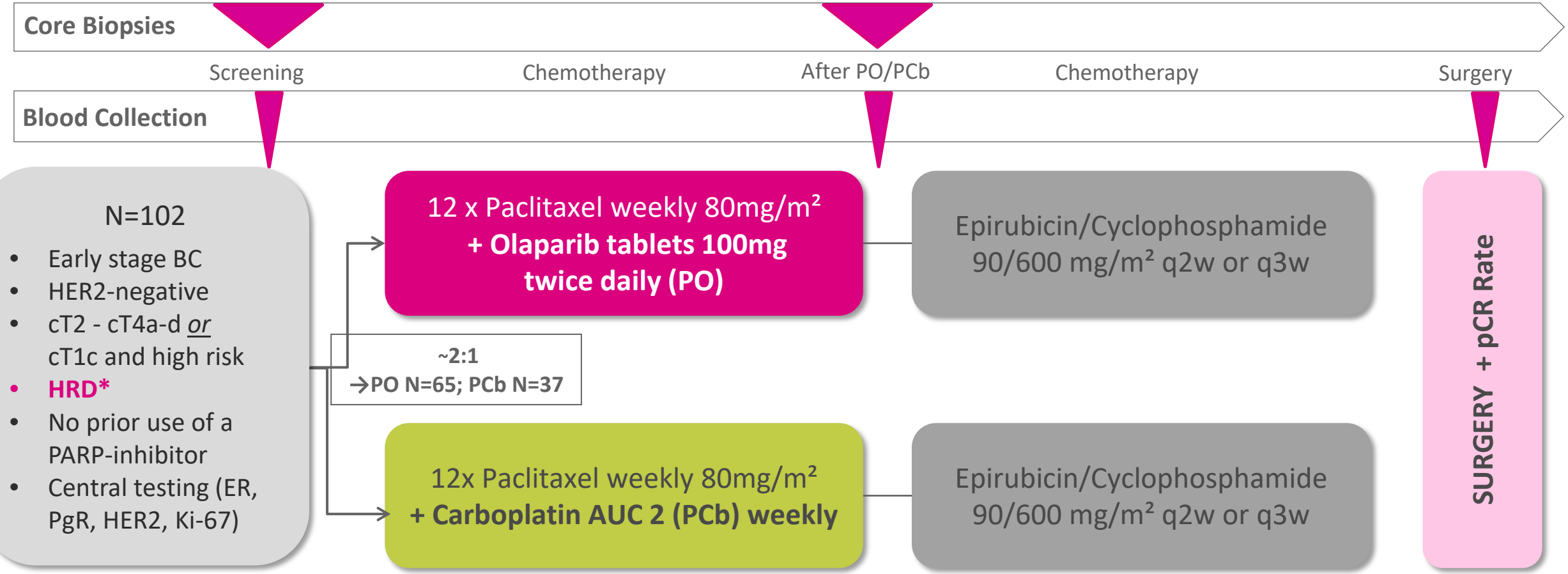
Peter A. Fasching

GeparOla Study Design



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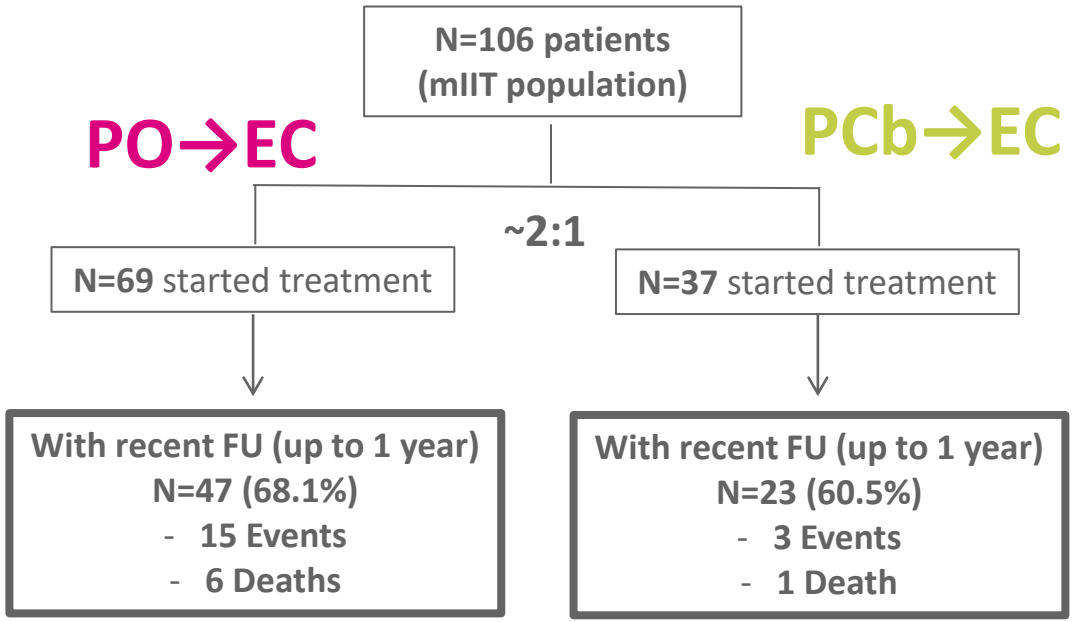
Patient Disposition and Patient Characteristics

Consort Diagram



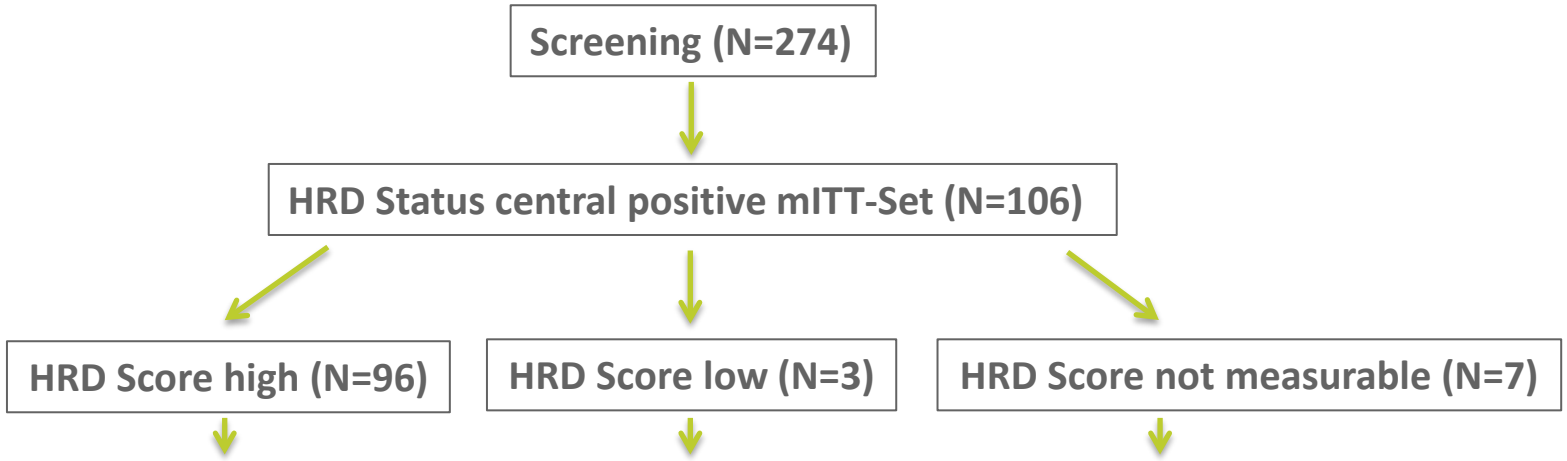
Main Baseline Characteristics

	PO→EC N=69 N (%) *	PCb→EC N=37 N (%) *	Overall N=106 N (%) *
Age (years), median (range)	48.0 (25.0, 71.0)	45.0 (26.0, 67.0)	47.0 (25.0, 71.0)
cT2	41 (60.3)	23 (62.2)	64 (61.0)
cN+	17 (24.5)	16 (45.7)	33 (31.8)
ER and/or PgR positive**	19 (27.5)	10 (27.0)	29 (27.4)
Ki-67 > 20%**	63 (91.3)	32 (86.5)	95 (89.6)
g/tBRCA-mutation	38 (55.9)	21 (56.8)	59 (56.2)

*valid percent
** central testing

Fasching et *al*. Ann Oncol. 2020

Screening for Patients: HRD Status and g/t*BRCA*1/2 Mutations



g/t*BRCA*	HRD Score high N (%)	HRD Score low N (%)	HRD Score not measurable* N (%)
Mutated (n=55)	49 (46.2)	3 (2.8)	3 (2.8)
Intact (n=46)	46 (43.4)	0 (0.0)	0 (0.0)
Not measurable*	1 (0.9)	0 (0.0)	4 (3.8)**

■ Eligible patients
* Insufficient quality or quantity of DNA
** Eligibility criteria: g*BRCA* local positive

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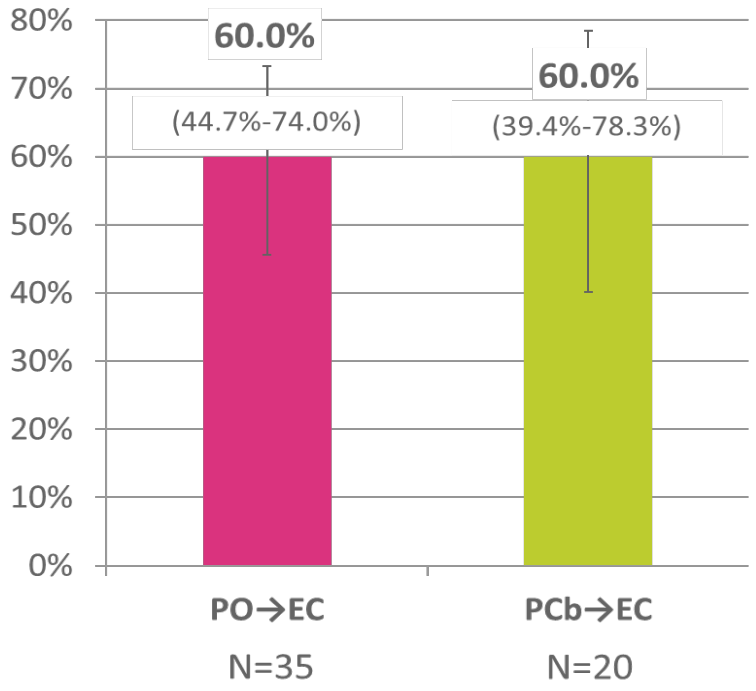
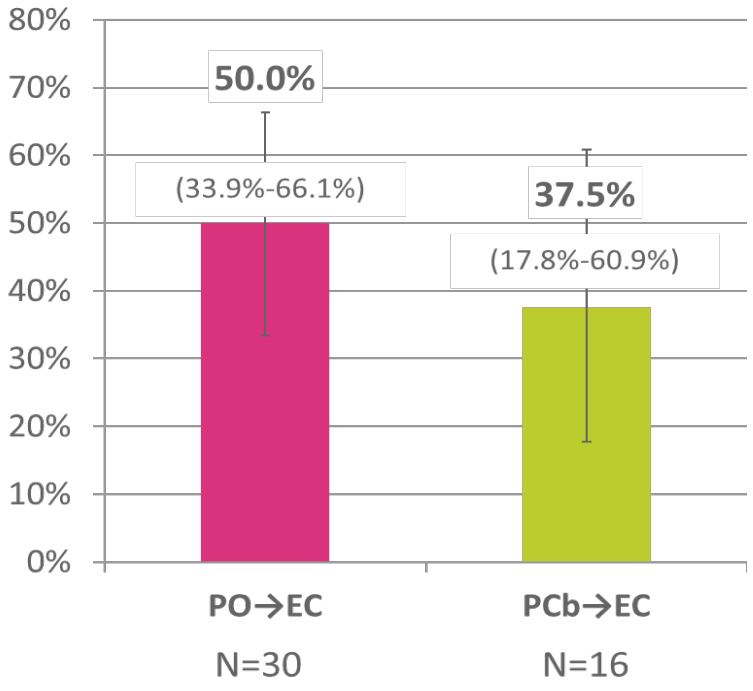
pCR Rates in *g/tBRCA* Subgroups

g/t*BRCA* mutated
(N=55)
(n=49 HRD high)



g/t*BRCA* wildtype
(N=46)
(all HRD high)



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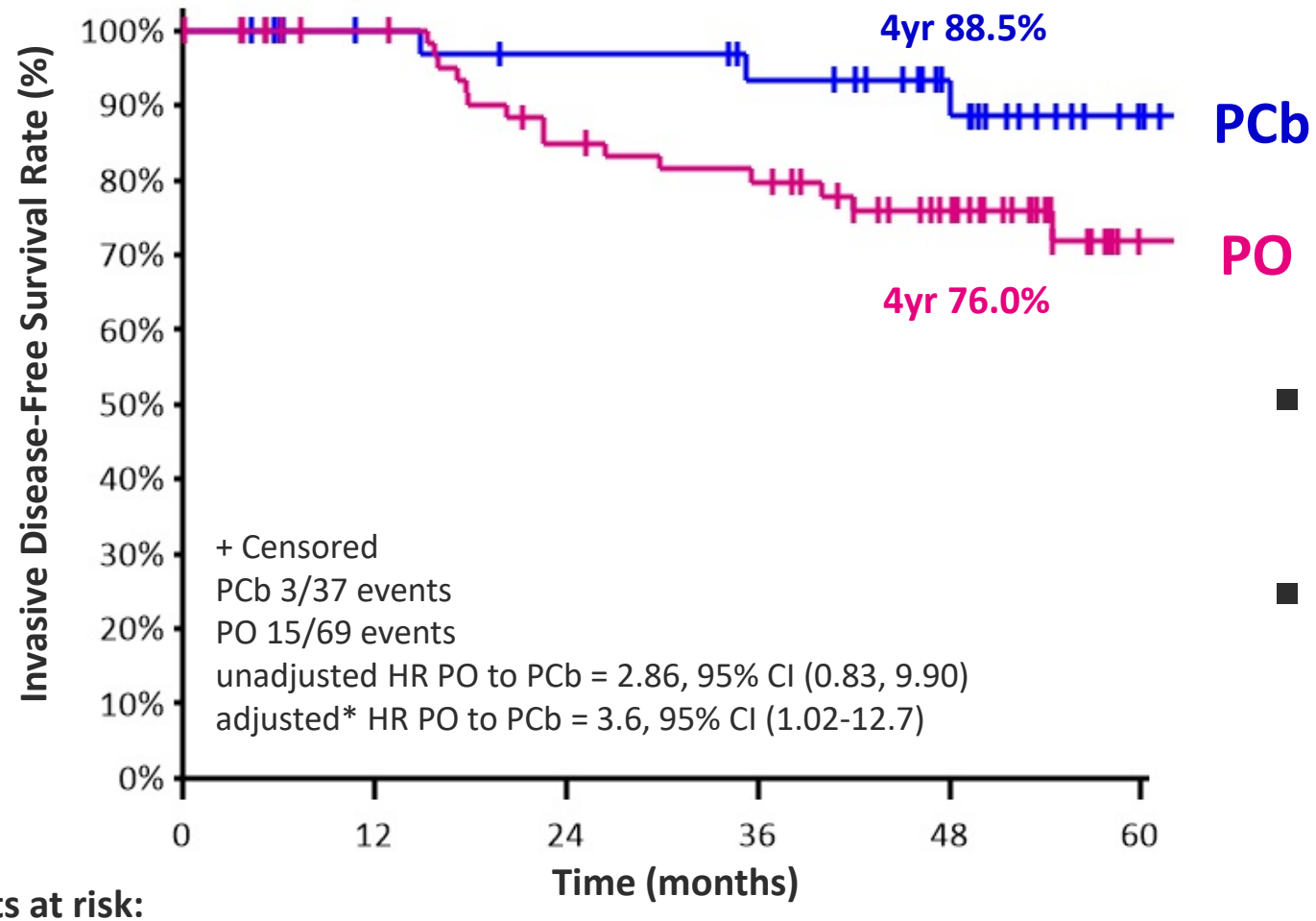
Methods for this Long-Term Efficacy Analysis

- **Long-term efficacy endpoints included**
  - Invasive disease-free survival (iDFS)
  - Distant disease-free survival (DDFS)
  - Overall survival (OS)

- **Statistical considerations:**
  - The time-to-event endpoints analysis was planned with a median follow-up of at least 4 years and a follow-up completeness of at least 80%
  - No adjustment for multiple testing

- Reported: - 18 iDFS events (15 in the PO arm and 3 in the PCb arm)
  - 13 DDFS events (11 in the PO arm and 2 in the PCb arm)
  - 7 death events (6 in the PO arm and 1 in the PCb arm)

Results: iDFS in the Overall Study Population



- Median follow-up of 49.8 (range 0.1 – 69.1) months
- 4-year loco-regional recurrence rate after PO treatment was higher (10.3%) compared to PCb treatment (4.9%)

*adjusted for nodal status and gene mutation status

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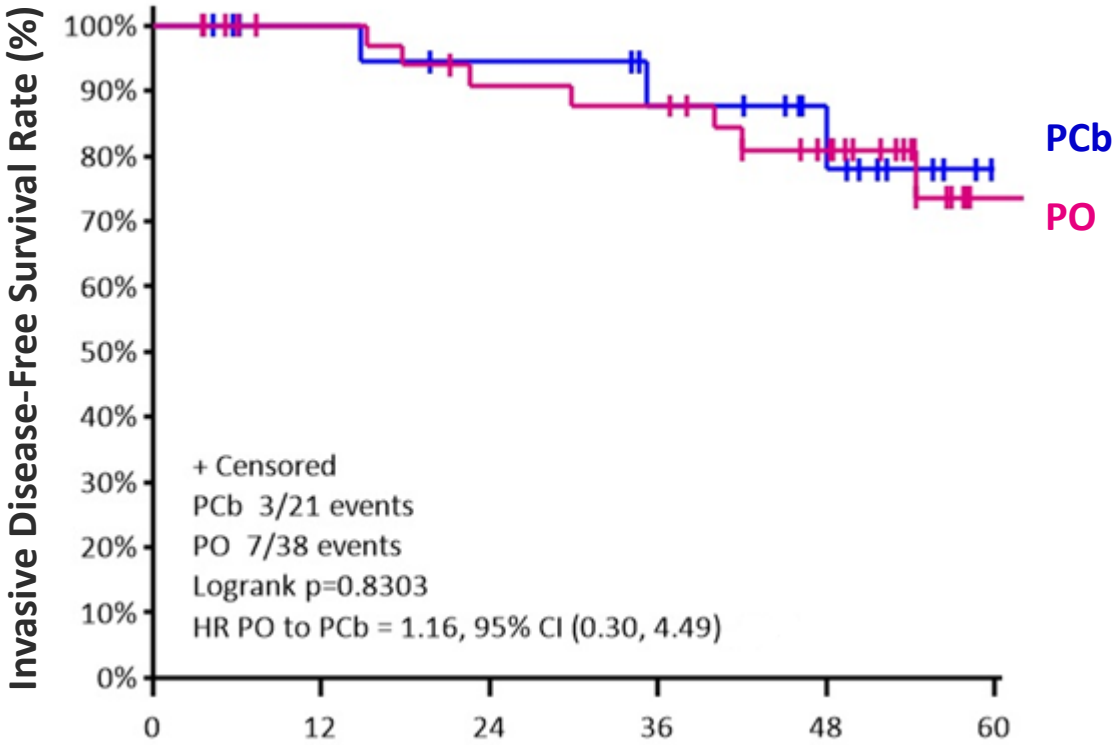
Results: iDFS Stratified by *BRCA*1/2-Mutation Status

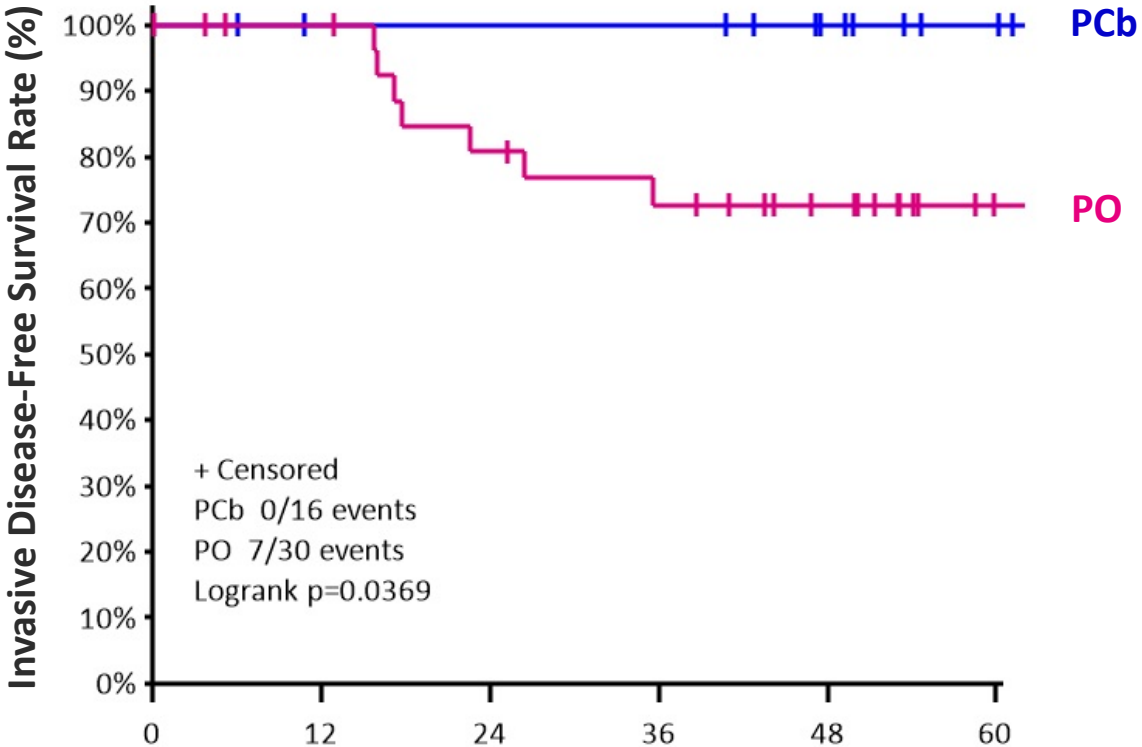
g/*tBRCA* mutated



Patients at risk:

PCb	21	18	16	13	9	0
PO	38	33	29	28	21	3

g/t*BRCA* wildtype (HRD score high)



Patients at risk:

PCb	16	14	14	14	10	6
PO	30	27	21	18	13	4

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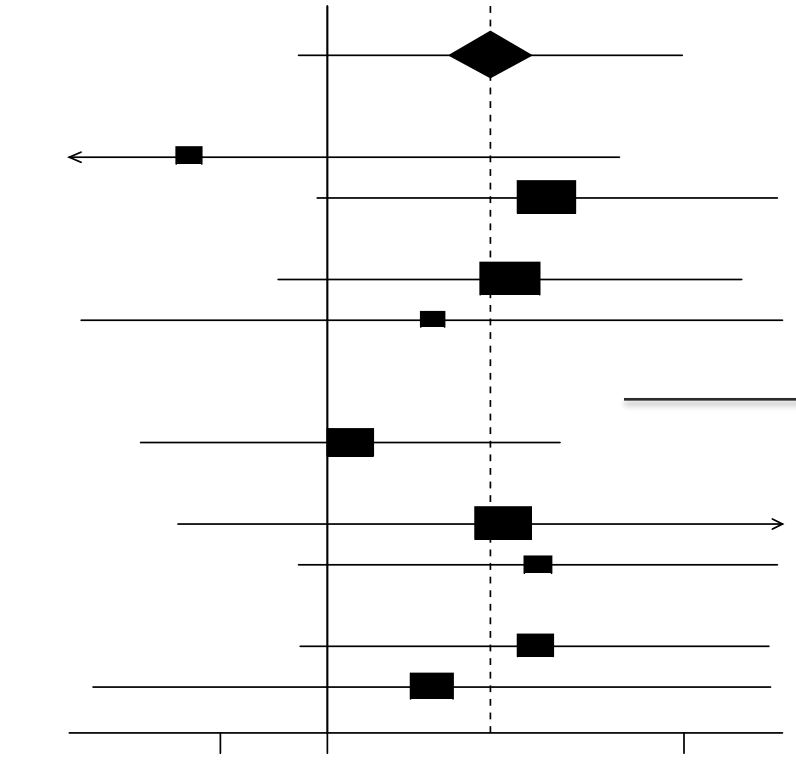
Results: Hazard Ratios According to Subgroups

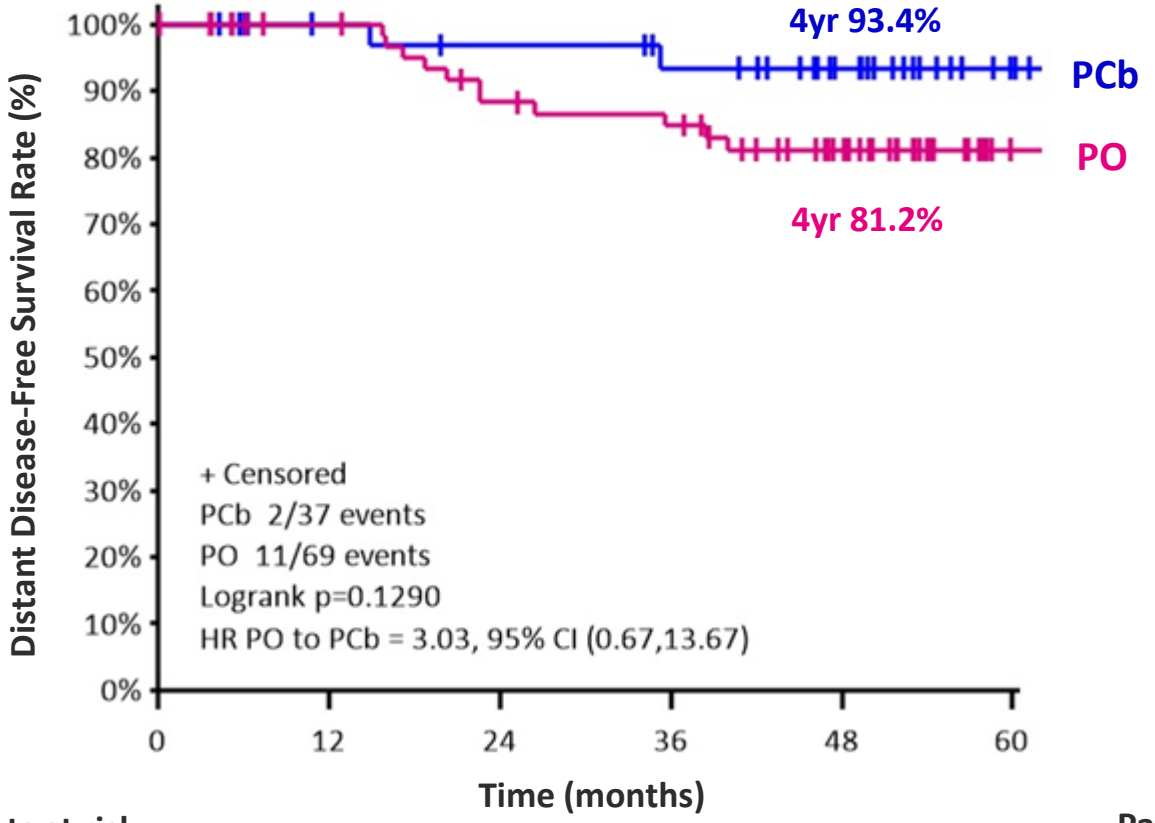
Subgroup	N patients	Hazard Ratio (95% CI)	p-Value	Test for Interaction
Overall	106	2.86 (.829, 9.90)	0.096	
				0.185
<40	32	.408 (.025, 6.62)	0.529	
>= 40	74	4.14 (.940, 18.2)	0.060	
hormone receptor status				0.722
HR-	77	3.26 (.728, 14.6)	0.122	
HR+	29	1.97 (.205, 19.0)	0.556	
g/tBRCA mutation				
negative	46	n.a.* (no events in PCb arm)		
positive	59	1.16 (.299, 4.49)	0.830	
cN				0.844
cN0	72	3.11 (.383, 25.3)	0.288	
cN+	33	3.91 (.828, 18.4)	0.085	
pCR (ypT0/is ypN0)				0.624
no	45	3.82 (.843, 17.3)	0.082	
yes	53	1.97 (.220, 17.6)	0.545	



Longer iDFS with Olaparib+Paclitaxel Longer iDFS with Carboplatin+Paclitaxel

Results: DDFS and OS in the Overall Study Population

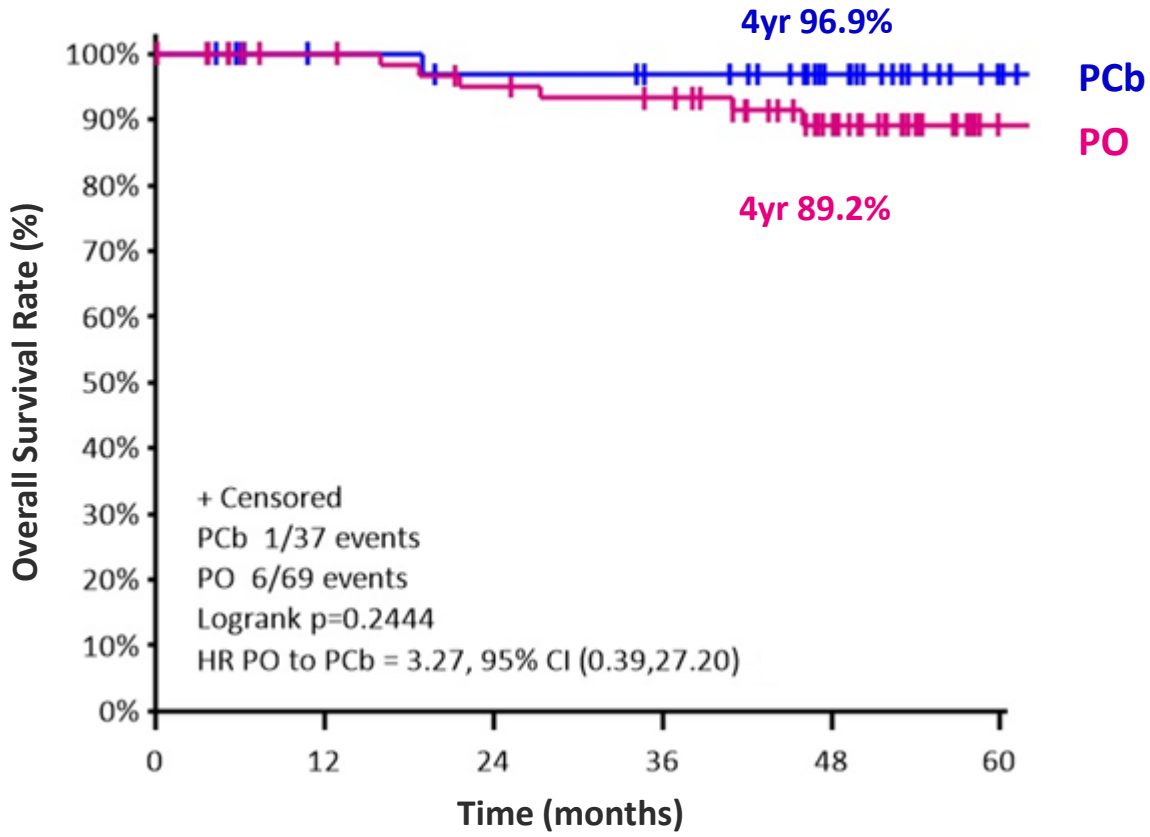
DDFS



Patients at risk:

PCb	37	32	30	27	19	6
PO	69	61	52	49	36	7

OS



Patients at risk:

PCb	37	32	30	28	19	6
PO	69	61	56	53	37	7

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Summary and Conclusion

- GeparOLA investigated the addition of olaparib to paclitaxel as part of a NACT in HER2 negative early BC patients with homologous recombination deficiency.
- The pCR rates were not different between the treatment arms.
- iDFS, DDFS and OS was numerically inferior with PO-EC compared to PCb-EC.
- iDFS between PO-EC and PCb-EC in patients with g/t*BRCA* mutation was comparable.

It can be hypothesized within the population of HER2 negative early BC patients with HRD:

- In patients with a g/t*BRCA* mutation olaparib can replace carboplatinum.
- In patients without a g/t*BRCA* mutation platinum containing NACT might result in a superior outcome.

These results need to be confirmed in a larger clinical trial!

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Patient Self-Registry

GBG

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