OlympiA

A Randomised, Double-blind, Parallel Group, Placebo-controlled Multi-centre Phase III Study to Assess the Efficacy and Safety of Olaparib Versus Placebo as Adjuvant Treatment in Patients With gBRCA1/2 Mutations and High Risk HER2-Negative Primary Breast Cancer Who Have Completed Definitive Local Treatment and Neoadjuvant or Adjuvant Chemotherapy

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1

Background

Over a quarter of people with early breast cancer will have their cancer return[1]

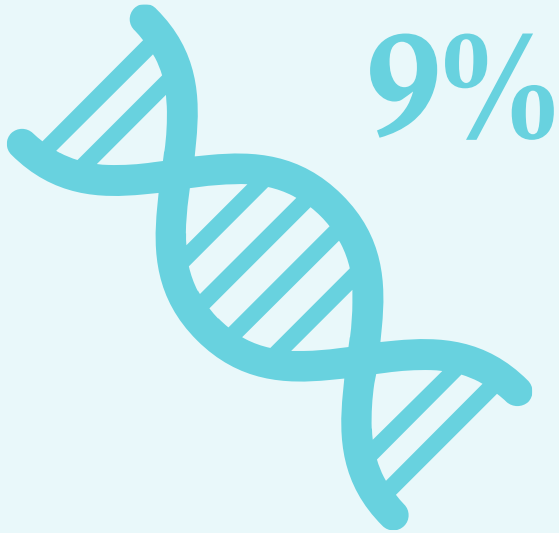
Breast cancer is the

most common

cancer worldwide[2]

20–30%* **will recur**

where cure is no longer possible[1]



~9% with HER2-negative disease have a **gBRCAm**[3,4]

ABBREVIATIONS

5 *Of patients diagnosed with early breast cancer

1. Riggio AI et al. *Br J Cancer*. 2021;124(1):13-26 1 2. Sung H et al. *CA Cancer J Clin*. 2021;71:209–249 3. De Talhouet S et al. *Sci Rep*. 2020;10:7073. 4. Winter C et al. Supplementary appendix. *Ann Oncol*. 2016;27:1532–1538.

Detection of a germline BRCAm significantly impacts a patient's care plan

Germline BRCAm breast cancer

Patients with gBRCA mutations are **often younger and present with aggressive disease**[1-3]

gBRCA status can **alter surgical decisions** and **therapeutic options**[4]

Many patients **do not meet common** gBRCA **testing criteria*** and may **miss the opportunity to benefit from targeted treatment**[5]

The OlympiA trial investigates olaparib as an adjuvant therapy for patients with gBRCAm, HER2-negative eBC who have a high risk of recurrence despite standard of care local and systemic therapy

*Such as family history or age of diagnosis

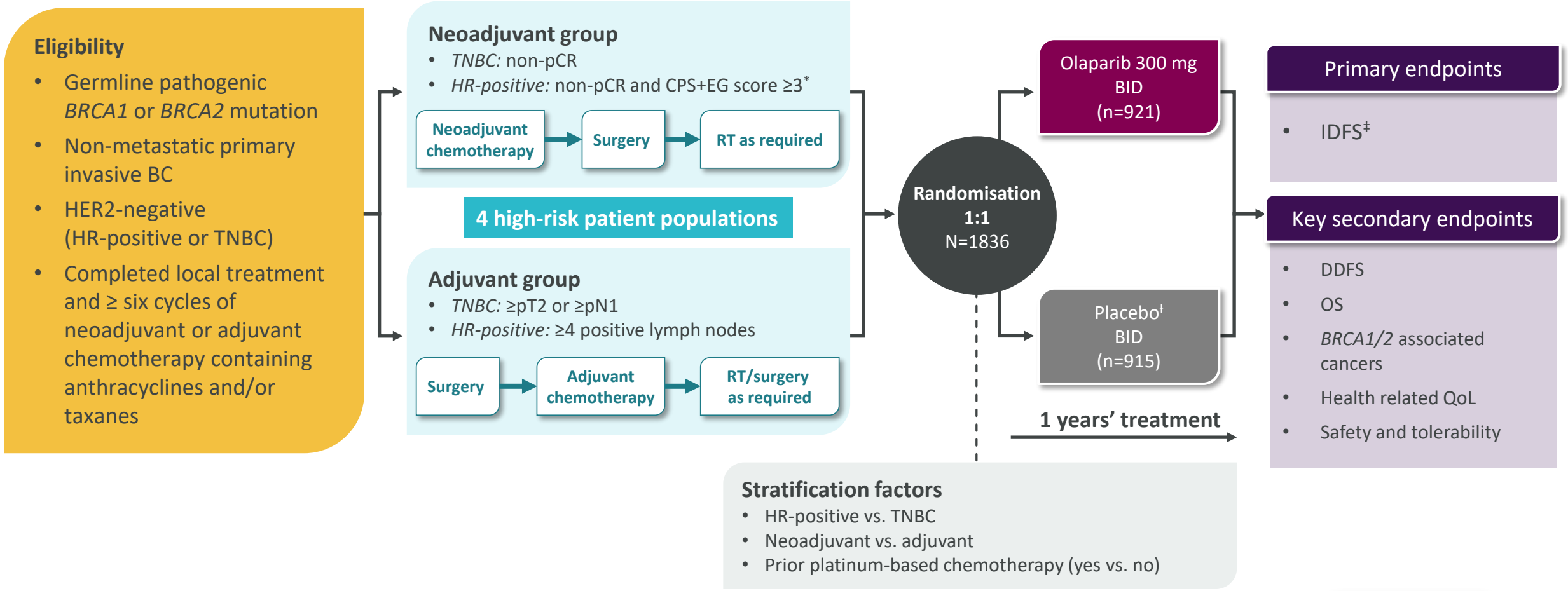
1. Baretta Z et al. *Medicine (Baltimore)*. 2016;95:e4975. 2. Aleskandarany M et al. *Breast Cancer Res Treat.* 2015;150:81–90. 3. Becourt S, et al. *J Clin Oncol*. 2018;36(suppl; abstr e13522). 4. Tung N *Br J Cancer*. 2018;119:141–152. 5. Rummel S, et al. *Cancers (Basel)*. 2020;12:234.

ABBREVIATIONS

2

Study design

OlympiA: Phase III study of olaparib versus placebo as adjuvant treatment for high risk gBRCA-mutated, HER2-negative BC



* CPS+EG score incorporates pretreatment clinical stage, oestrogen receptor status, nuclear grade and pathological stage after neoadjuvant chemotherapy

† Data to support adjuvant capecitabine was not available when the OlympiA study was initiated in 2014

‡ by STEEP system[2]

1. Tutt ANJ et al. *N Engl J Med.* 2021;384:2394-2405. 2.Hudis CA. *J Clin Oncol.* 2007;25:2127–2132.

ABBREVIATIONS

A multiple testing procedure was adopted

IDFS primary analysis 165 IDFS events in mature cohort[1] (ASCO 2021)	Second OS interim analysis 330 IDFS events in ITT[2] (ESMO Virtual Plenary 2022)	DDFS and OS analysis 10 years from FPI[3] (SABCS 2024)
DCO1: 27 March 2020[1]	DCO2: 12 July 2021[2]	DCO3: 05 June 2024[3]
Invasive disease-free survival p<0.005	Invasive disease-free survival descriptive	Invasive disease-free survival descriptive
Distant disease-free survival p<0.005	Distant disease-free survival descriptive	Distant disease-free survival descriptive
Overall survival p<0.01	Overall survival p<0.015	Overall survival descriptive
Median follow-up[1]: ITT population: 2.5 years Mature cohort: 3.5 years	**Median follow-up[2]:** ITT population: 3.5 years	**Median follow-up[3]:** ITT population: 6.1 years Maximum follow-up: 9.6 years

DDFS and OS will only be tested if IDFS is significant

If DDFS is significant, OS will be tested at p<0.01

Significance boundaries were crossed for IDFS and DDFS at the prior planned interim analysis IDFS and for OS at OS interim analysis. No further significance testing was performed

ABBREVIATIONS

1. Tutt ANJ et al. Supplementary Appendix *N Engl J Med.* 2021;384:2394-2405. 2. Geyer C, Garber J, Gelber R et al. *Annals of Oncology*. 2022;33(12):1250-1268. 3. Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

3

Patient disposition and baseline characteristics

Baseline characteristics were well balanced between treatment groups

	Olaparib n=921	Placebo n=915
Age – years, median (interquartile range), *years*	42 (36–49)	43 (36–50)
Female, ***n (%)***	919 (99.8)	911 (99.6)
BRCA gene affected in germline, *n (%)*		
BRCA1	657 (71.3)	670 (73.2)
BRCA2	261 (28.3)	239 (26.1)
BRCA1 & *BRCA2*	2 (0.2)	5 (0.5)
Missing	1 (0.1)	1 (0.1)
Menopausal status (females only), *n (%)*		
Premenopausal	572/919 (62.2)	552/911 (60.6)[2]
Postmenopausal	347/919 (37.8)	359/911 (39.4)[2]
Bilateral invasive breast cancer, *n (%)*		
No	881 (95.7)	888 (97.0)
Yes	40 (4.3)	27 (3.0)

ABBREVIATIONS

1. Tutt ANJ et al. *N Engl J Med.* 2021; 384:2394-2405. 2. Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

Approximately 80% of patients had TNBC

	Olaparib n=921	Placebo n=915
Prior (neo)adjuvant chemotherapy, *n (%)* [*]		
Adjuvant	461 (50.1)	455 (49.7)
Neoadjuvant		460 (50.3)
Anthracycline and taxane regimen		850 (92.9)[2]
Anthracycline regimen (without taxa		13 (1.4)
Taxane regimen (without anthracycli		52 (5.7)
(Neo)adjuvant platinum-based chemoth		
No		677 (74.0)
Yes		238 (26.0)
HR status, *n (%)* [†]		
HR-positive / HER2-negative		157 (17.2)
TNBC[‡]		758 (82.8)
Concurrent hormone therapy (HR-positive only), *n/N (%)*	146/168 (86.9)	146/157 (93.0)[2]

Protocol amendment

The original protocol activated in 2014 was developed for patients with HER2-negative disease but included only patients with TNBC following a regulatory review.

The first patient with HR-positive disease was enrolled in December 2015.

[*]7 patients in the Olaparib arm and 15 patients in the placebo arm received less than 6 cycles of (neo)adjuvant chemotherapy. Regimen for 1 patients in the placebo arm was not reported. All reported as protocol deviations; [†]Defined by local test results; [‡]TNBC: ER- and PgR-negative defined as IHC nuclear staining <1% AND HER2-negative (not eligible for anti-HER2 therapy) defined as IHC 0, 1+ without ISH OR IHC 2+ and ISH non-amplified with ratio <2.0 and, if reported, average HER2 copy number <4 signals/cell OR ISH non-amplified with ratio <2.0 and, if reported, average HER2 copy number <4 signals/cell (without IHC). Two patients were excluded from the summary of the TNBC subset because they did not have a confirmed HER2-negative status

1. Tutt ANJ et al. *N Engl J Med.* 2021; 384:2394-2405. 2. Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

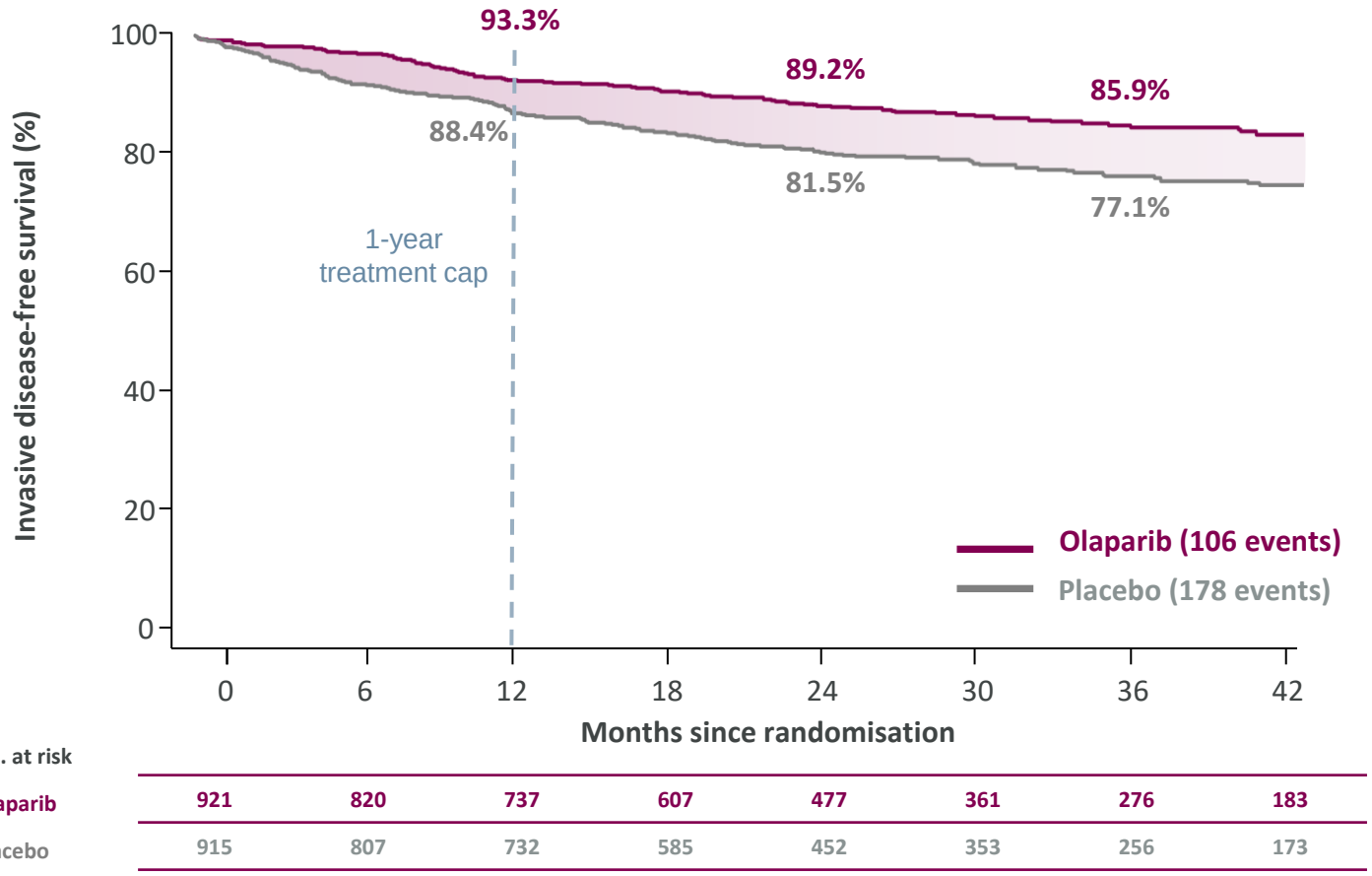
PROTOCOL AMENDMENT ABBREVIATIONS

4

Efficacy outcomes

Olaparib reduced the risk of invasive recurrence or death by 42% vs. placebo

Primary endpoint: invasive disease-free survival



No. at risk								
Olaparib	921	820	737	607	477	361	276	183
Placebo	915	807	732	585	452	353	256	173

IDFS at DCO1‡

HR 0.58†
99.5% CI 0.41–0.82
p<0.001

3-year IDFS rate*

Olaparib (n=921)	**85.9%**
Placebo (n=915)	**77.1%**

Difference 8.8%
95% CI 4.5–13.0

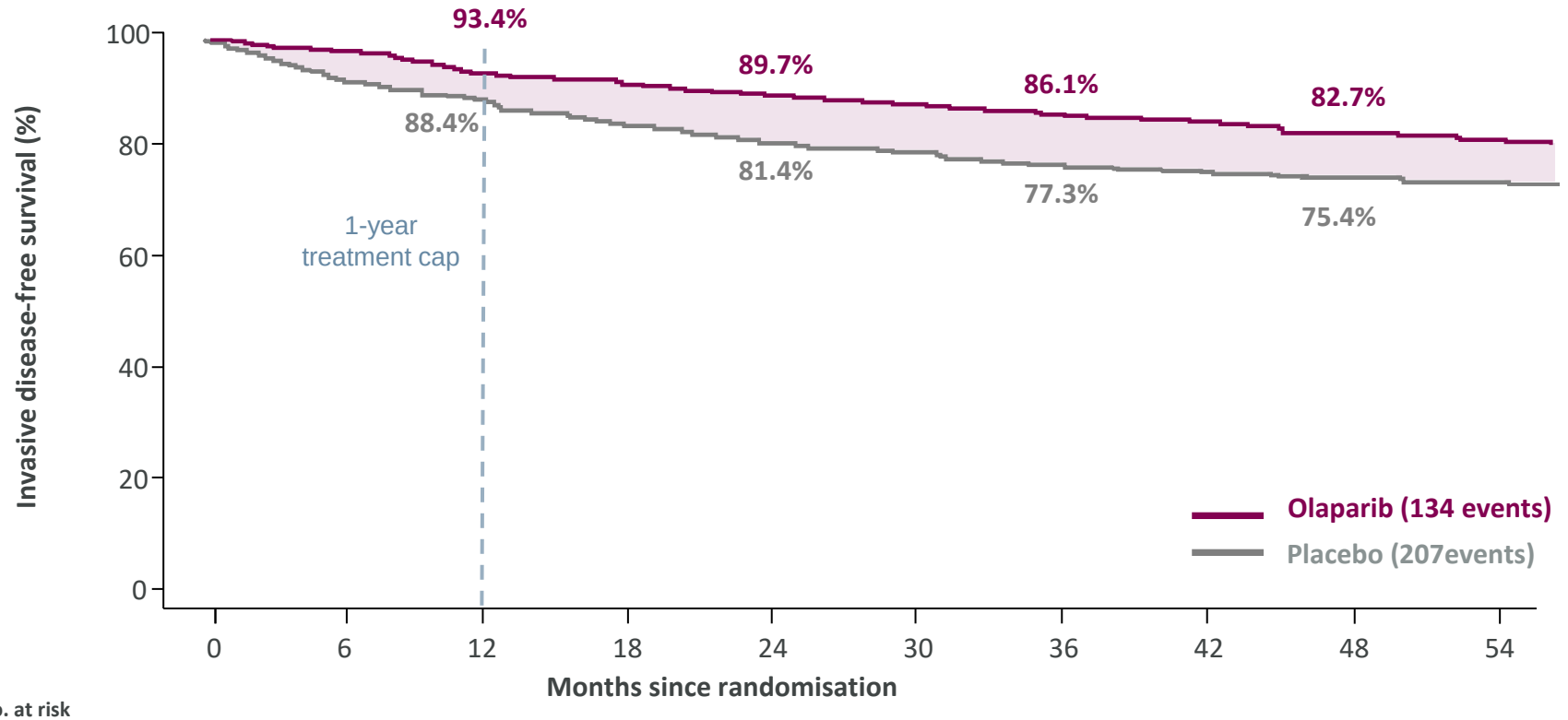
*Kaplan–Meier estimates; †Stratified Cox proportional hazards model; 99.5% CIs are shown for the HR because p<0.005 was required to indicate statistical significance for this endpoint; ‡DCO1 27 March 2020 (at 284 IDFS events, 15% data maturity ; median follow-up 2.5 years

Tutt ANJ et al. *N Engl J Med.* 2021; 384:2394-2405.

ABBREVIATIONS

IDFS benefit associated with olaparib was maintained with 1-year additional follow-up* (DCO2)

Exploratory analysis: invasive disease-free survival (descriptive)



No. at risk										
Olaparib	921	825	777	738	694	603	495	382	293	204
Placebo	915	807	765	715	656	571	459	370	293	187

IDFS at DCO2*

HR 0.63
95% CI 0.50–0.78

4-year IDFS rate

Olaparib (n=921) **82.7%**

Placebo (n=915) **75.4%**

Difference 7.3%
95% CI 3.0–11.5

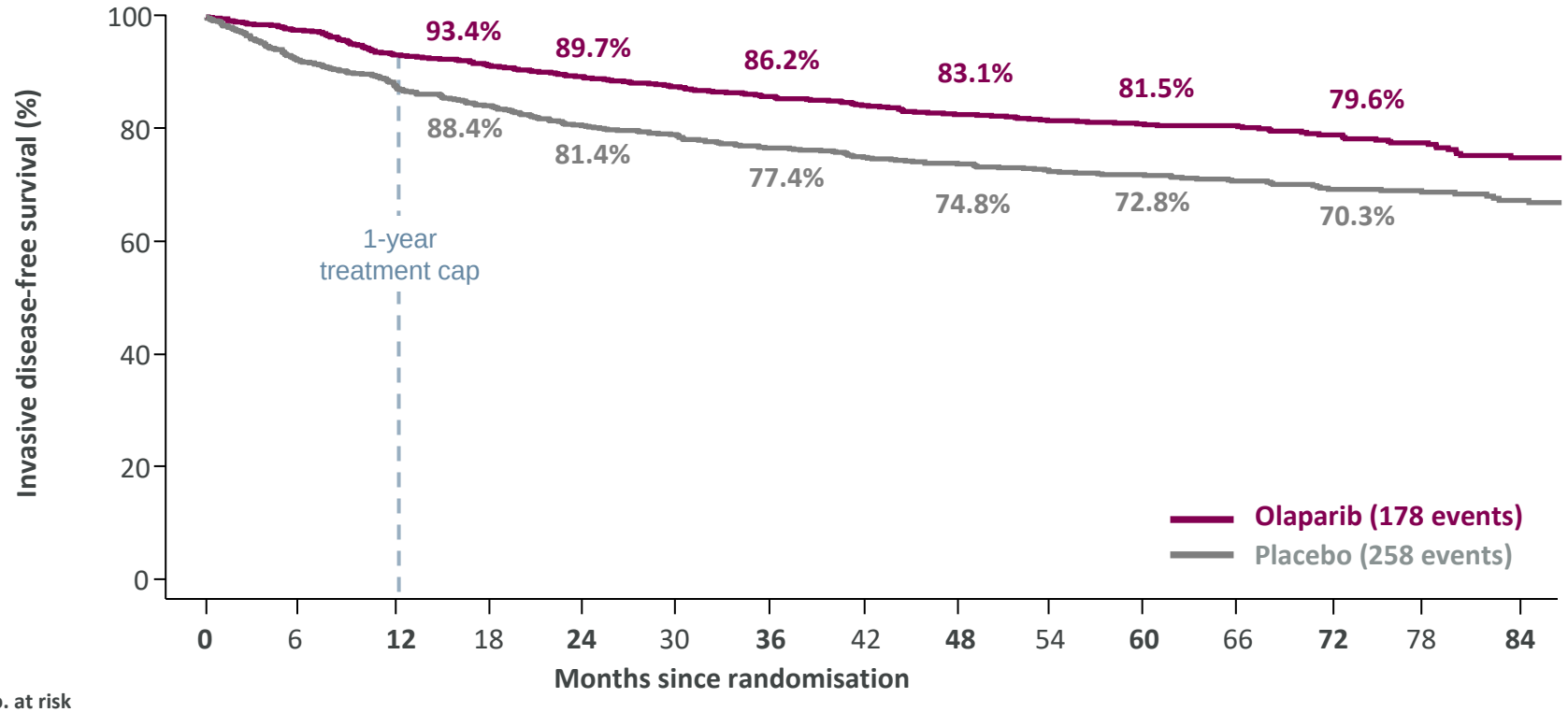
ABBREVIATIONS

*IDFS analysis is descriptive at OS IA2; ‡DCO2 12 July 2021 (at 330 IDFS events, 25% data maturity); median follow-up 3.5 years

2. Geyer C, Garber J, Gelber R et al. *Annals of Oncology*. 2022;33(12):1250-1268.

At 6.1 years median follow-up, one year of adjuvant olaparib after (neo)adjuvant chemotherapy continues to demonstrate clinically meaningful improvements in IDFS

Exploratory analysis: invasive disease-free survival (descriptive)



No. at risk								
Olaparib	921	778	712	670	632	570	361	194
Placebo	915	766	683	628	588	512	327	181

IDFS at DCO3

HR 0.65
95% CI 0.53–0.78

6-year IDFS rate

Olaparib (n=921)	**79.6%**
Placebo (n=915)	**70.3%**

Difference 9.4%
95% CI 5.1–12.7

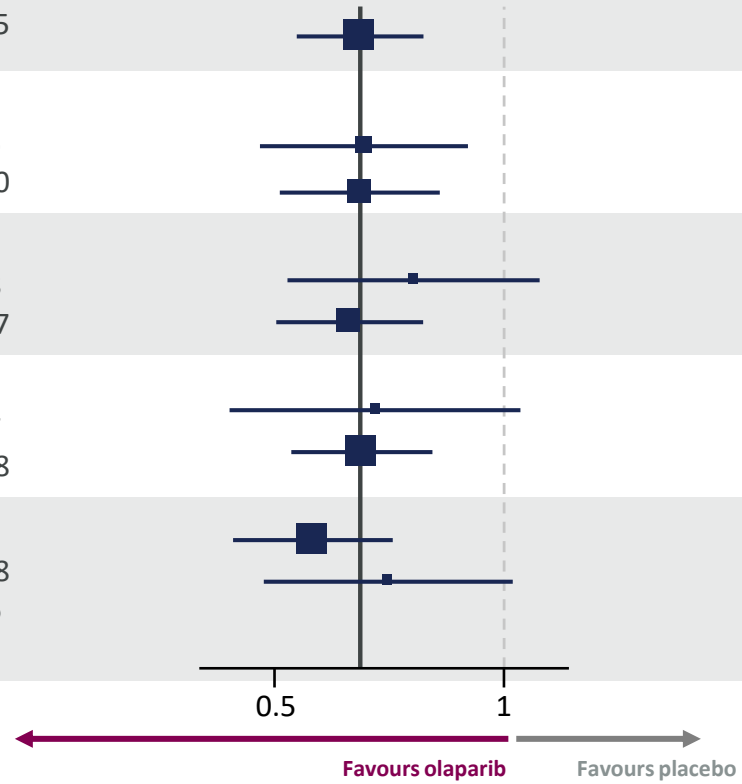
ABBREVIATIONS

DCO3 June 2024; median follow-up 6.1 years.

Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

A consistent benefit was seen across key IDFS subgroups at DCO3

Subgroup	Olaparib	Placebo	Stratified hazard ratio for OS (95% CI)	P value for heterogeneity
	No. of patients who died /total no.			
All patients	178 / 921	258 / 915	0.648 (0.535 – 0.784)	NA
Prior chemo				
Adjuvant	65 / 461	98 / 455	0.657 (0.479 - 0.897)	0.94
Neoadjuvant	113 / 460	160 / 460	0.648 (0.508 - 0.823)	
Prior platinum				
Yes	48 / 247	60 / 238	0.763 (0.520 - 1.113)	0.39
No	130 / 674	198 / 677	0.628 (0.503 - 0.783)	
HR status				
HR-positive/HER2-negative	35 / 168	47 / 157	0.681 (0.437 - 1.051)	0.86
TNBC	142 / 751	211 / 758	0.652 (0.526 - 0.805)	
BRCA				
BRCA1	106 / 579	177 / 588	0.563 (0.441 - 0.715)	0.61
BRCA2	49 / 235	62 / 216	0.707 (0.484 – 1.026)	
BRCA1 and *BRCA2*	0 / 2	0 / 3	NC	



DCO3 June 2024; median follow-up 6.1 years.

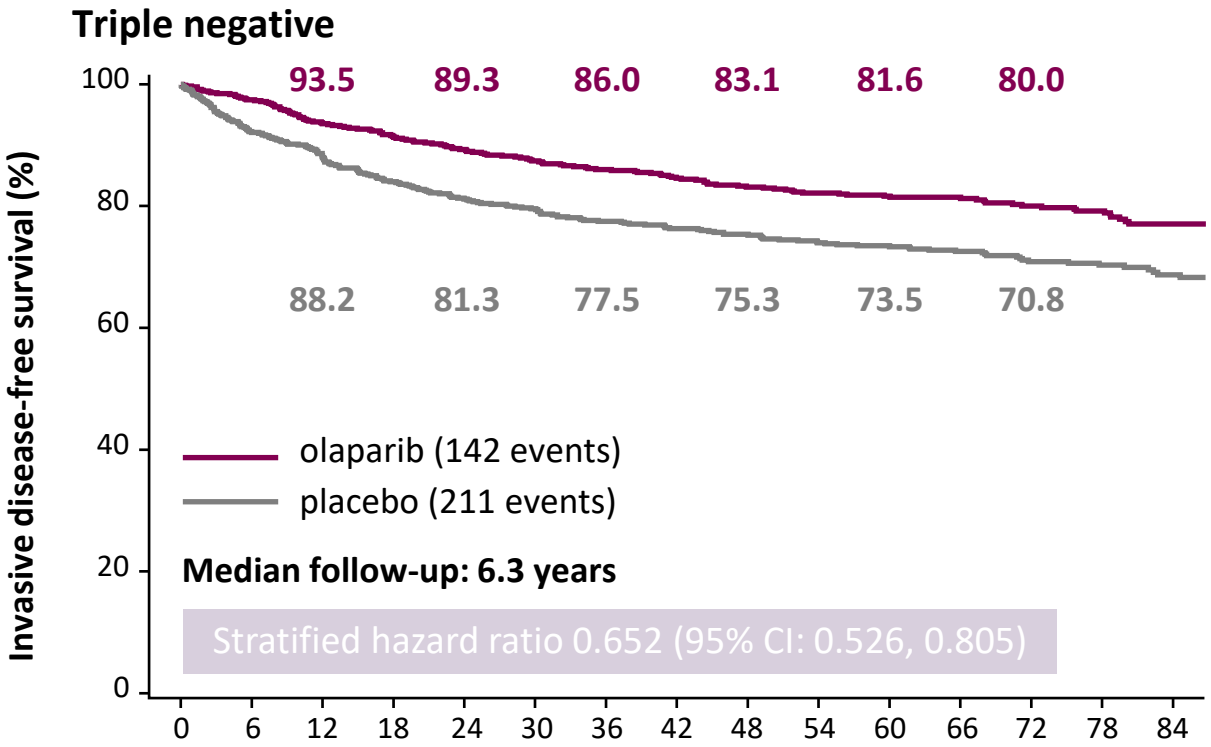
All subgroup hazard ratio estimates are <1 and all confidence intervals include the ITT population hazard ratio (shown by solid red vertical line as per Cuzick J., Lancet 2005; 365:1308)

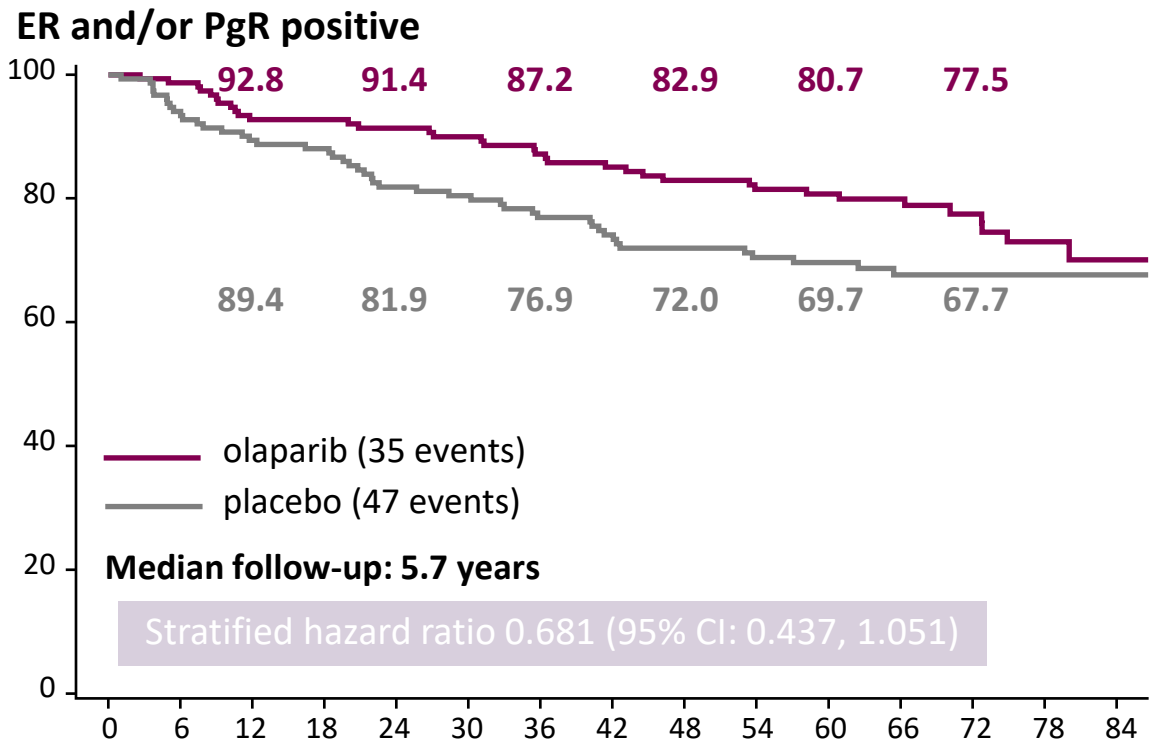
ABBREVIATIONS

Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

Olaparib benefit was consistent across all key subgroups, including for patients with high-risk, ER and/or PgR positive disease

The TNBC cohort (82% of randomized patients and with >6 years MFU) is relatively more mature





Number at risk								
Olaparib	751	636	579	544	514	463	306	178
Placebo	758	632	565	519	489	430	282	162

Time since randomisation (months)								
Olaparib	168	140	131	124	116	105	53	15
Placebo	157	134	118	109	99	82	45	19

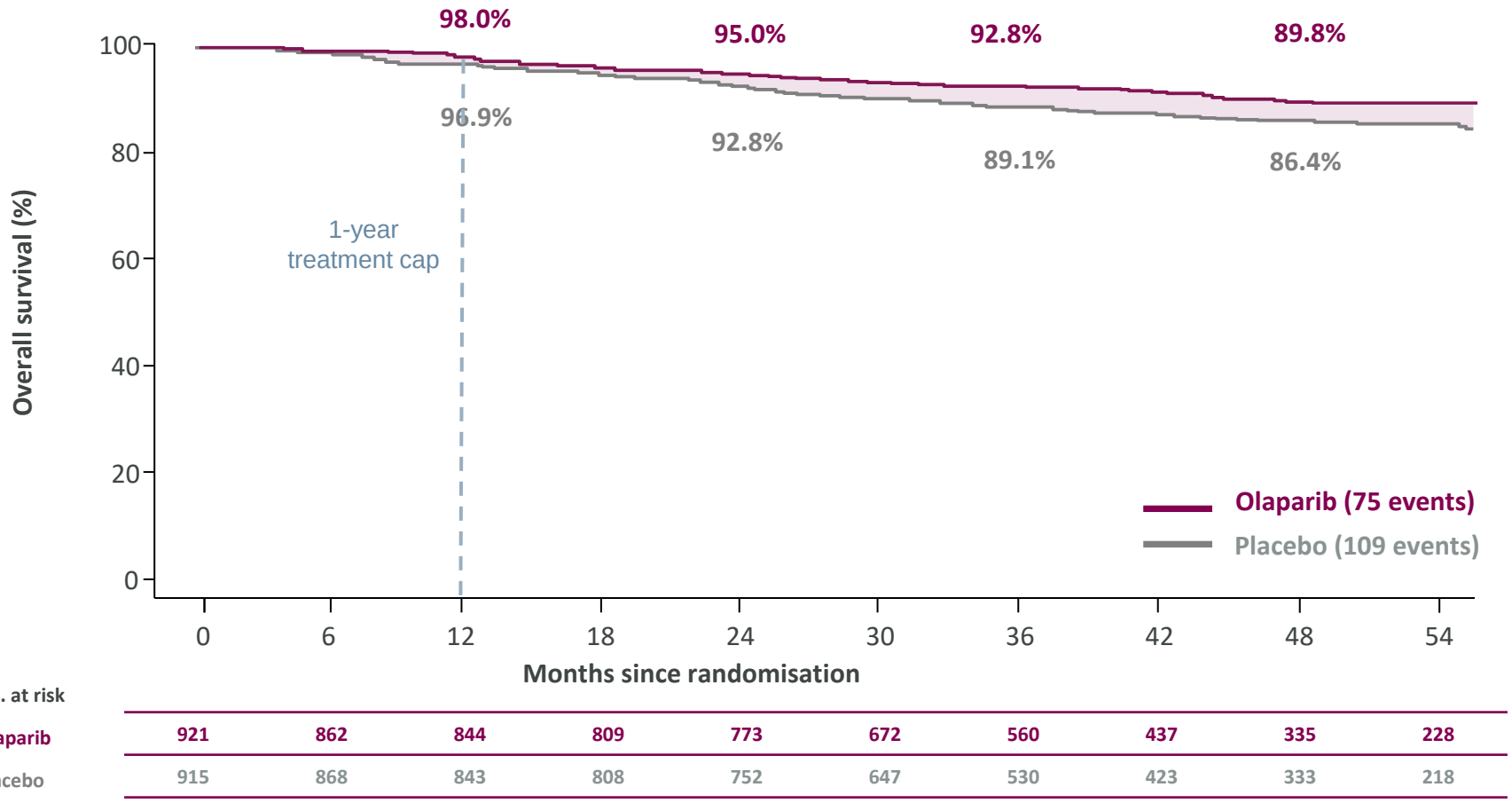
ABBREVIATIONS

DCO3 June 2024.

Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

Olaparib demonstrated a significant OS benefit vs. placebo with 90% of patients alive at 4-years in the olaparib arm

Secondary endpoint: overall survival



No. at risk										
Olaparib	921	862	844	809	773	672	560	437	335	228
Placebo	915	868	843	808	752	647	530	423	333	218

OS at DCO2*

HR 0.68†
98.5% CI 0.47–0.97
p=0.009

4-year OS rate

Olaparib (n=921) **89.8%**

Placebo (n=915) **86.4%**

Difference 3.4%
95% CI -0.1–6.8

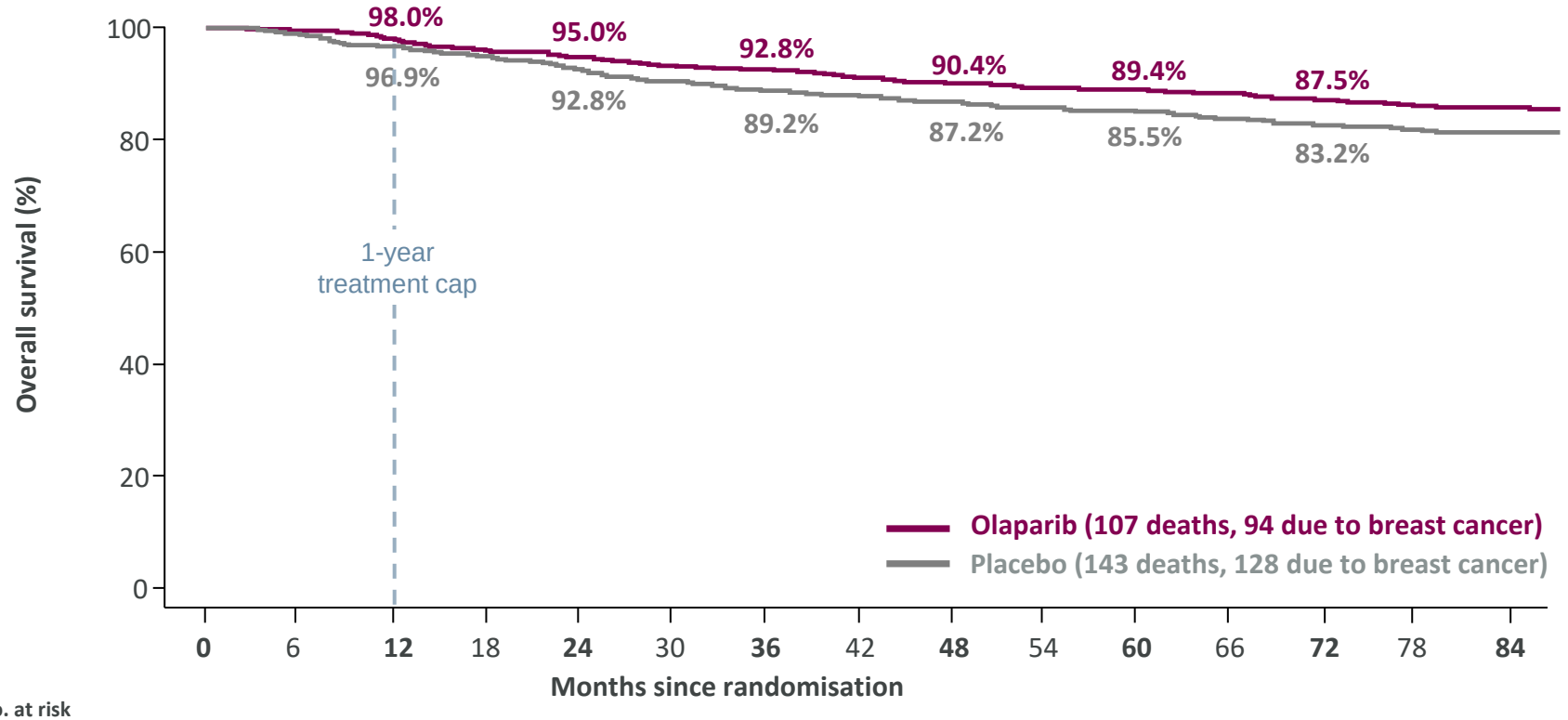
*Data from the pre-specified second interim analysis of OS (at ~330 IDFS events); cut-off date July 2021 (DCO2), data maturity 9%; median follow-up 3.5 years; †Non-proportional hazards; 98.5% CI is shown for the HR for OS because p<0.015 is required to indicate statistical significance for this endpoint

1. Geyer C, Garber J, Gelber R et al. *Annals of Oncology*. 2022;33(12):1250-1268. 2. In House Data, AstraZeneca. Data on file SD-2020-ALL-0088.

ABBREVIATIONS

Olaparib continued to demonstrate OS benefit vs. placebo at 6-years in the olaparib arm

Secondary endpoint: overall survival



No. at risk								
Olaparib	921	846	795	765	728	660	420	224
Placebo	915	843	788	739	698	616	390	221

OS at DCO3

HR 0.72
95% CI 0.56–0.93

6-year OS rate

Olaparib (n=921) **87.5%**

Placebo (n=915) **83.2%**

Difference 4.4%
95% CI 0.9–6.7

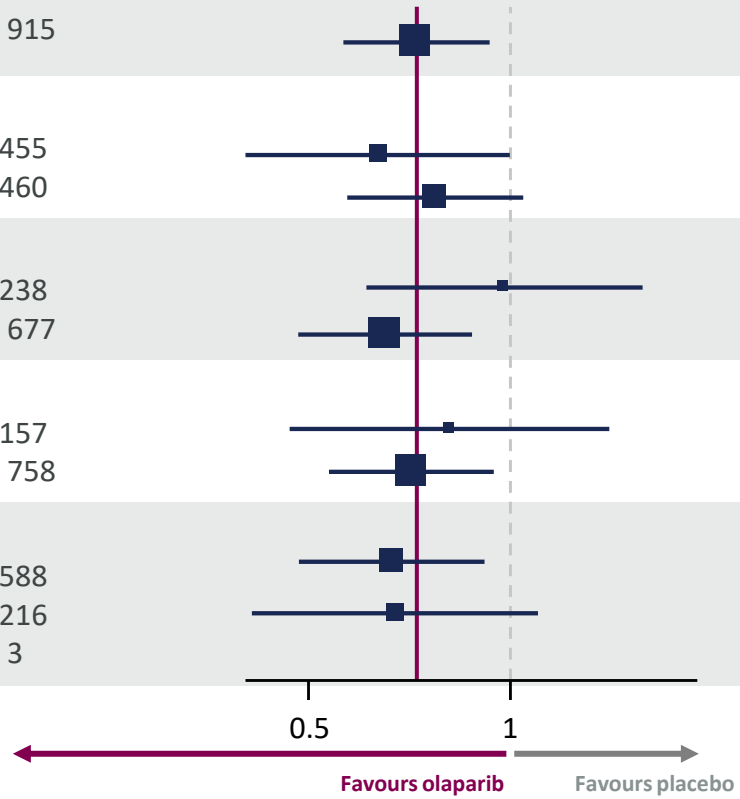
ABBREVIATIONS

DCO3 June 2024; median follow-up 6.1 years.

Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

OS benefit was derived across key subgroups (DCO3)

Subgroup	Olaparib	Placebo	Stratified hazard ratio for OS (95% CI)	P value for heterogeneity
	No. of patients who died /total no.			
All patients	107 / 921	143 / 915	0.725 (0.563 – 0.930)	NA
Prior chemo				
Adjuvant	31 / 461	48 / 455	0.638 (0.402 - 0.997)	0.49
Neoadjuvant	76 / 460	95 / 460	0.774 (0.571 – 1.045)	
Prior platinum				
Yes	35 / 247	34 / 238	0.979 (0.610 - 1.574)	0.15
No	72 / 674	109 / 677	0.653 (0.483 - 0.876)	
HR status				
HR-positive/HER2-negative	24 / 168	28 / 157	0.814 (0.469 - 1.404)	0.67
TNBC	83 / 751	115 / 758	0.713 (0.536 - 0.944)	
BRCA				
BRCA1	64 / 579	94 / 588	0.667 (0.484 - 0.914)	1.00
BRCA2	28 / 235	38 / 216	0.676 (0.412 – 1.098)	
BRCA1 and *BRCA2*	0 / 2	0 / 3	NC	



DCO3 June 2024; median follow-up 6.1 years.

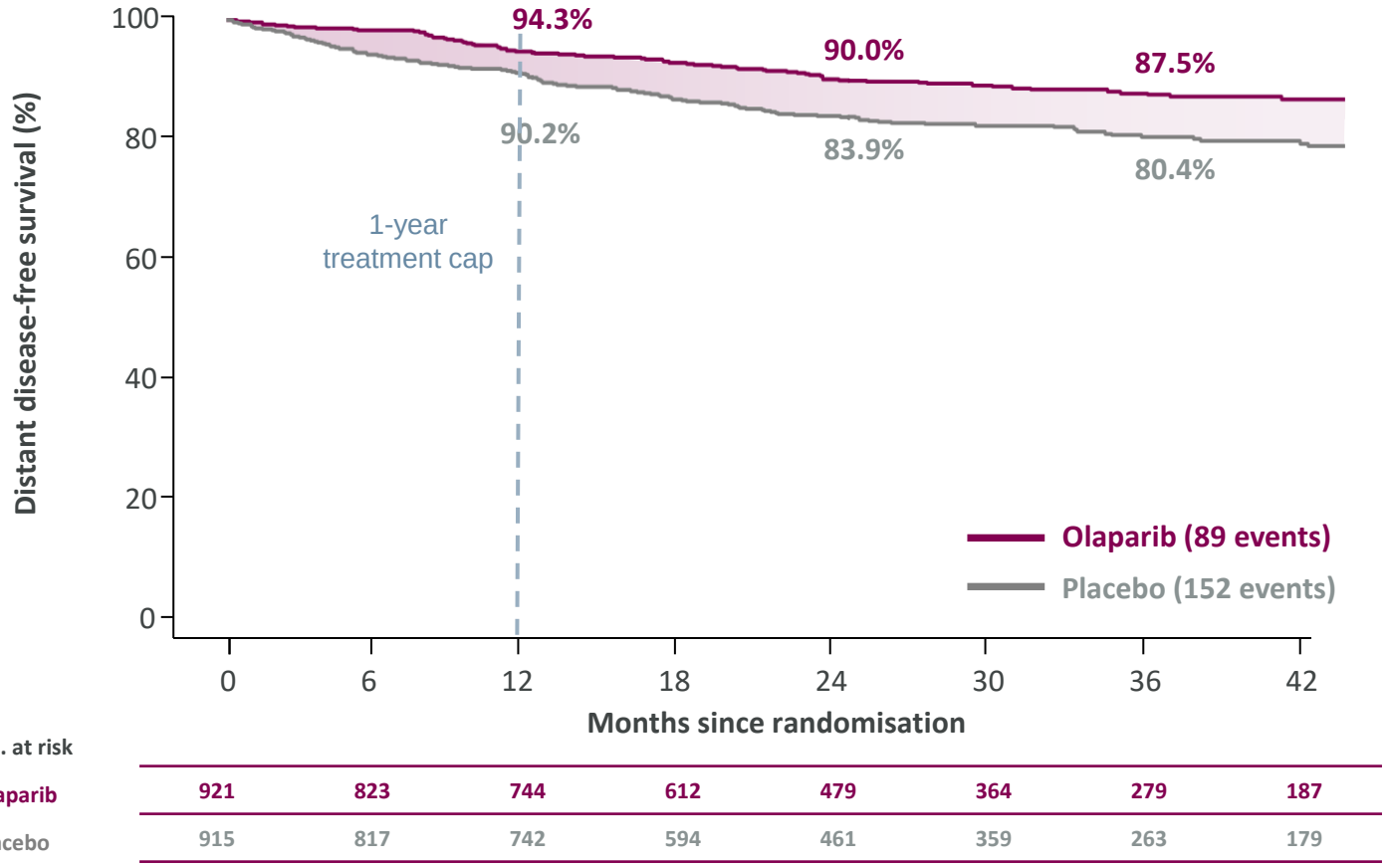
All subgroup hazard ratio estimates are <1 and all confidence intervals include the ITT population hazard ratio (shown by solid red vertical line as per Cuzick J., Lancet 2005; 365:1308)

ABBREVIATIONS

Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

Over 7% more patients treated with adjuvant olaparib were free of distant recurrence or death at 3 years vs. placebo

Secondary endpoint: distant disease-free survival



No. at risk								
Olaparib	921	823	744	612	479	364	279	187
Placebo	915	817	742	594	461	359	263	179

DDFS at DCO1*

HR 0.57 †
99.5% CI, 0.39–0.83
P<0.001

3-year DDFS rate

Olaparib (n=921)	**87.5%**
Placebo (n=915)	**80.4%**

Difference 7.1%
95% CI, 3.0–11.1

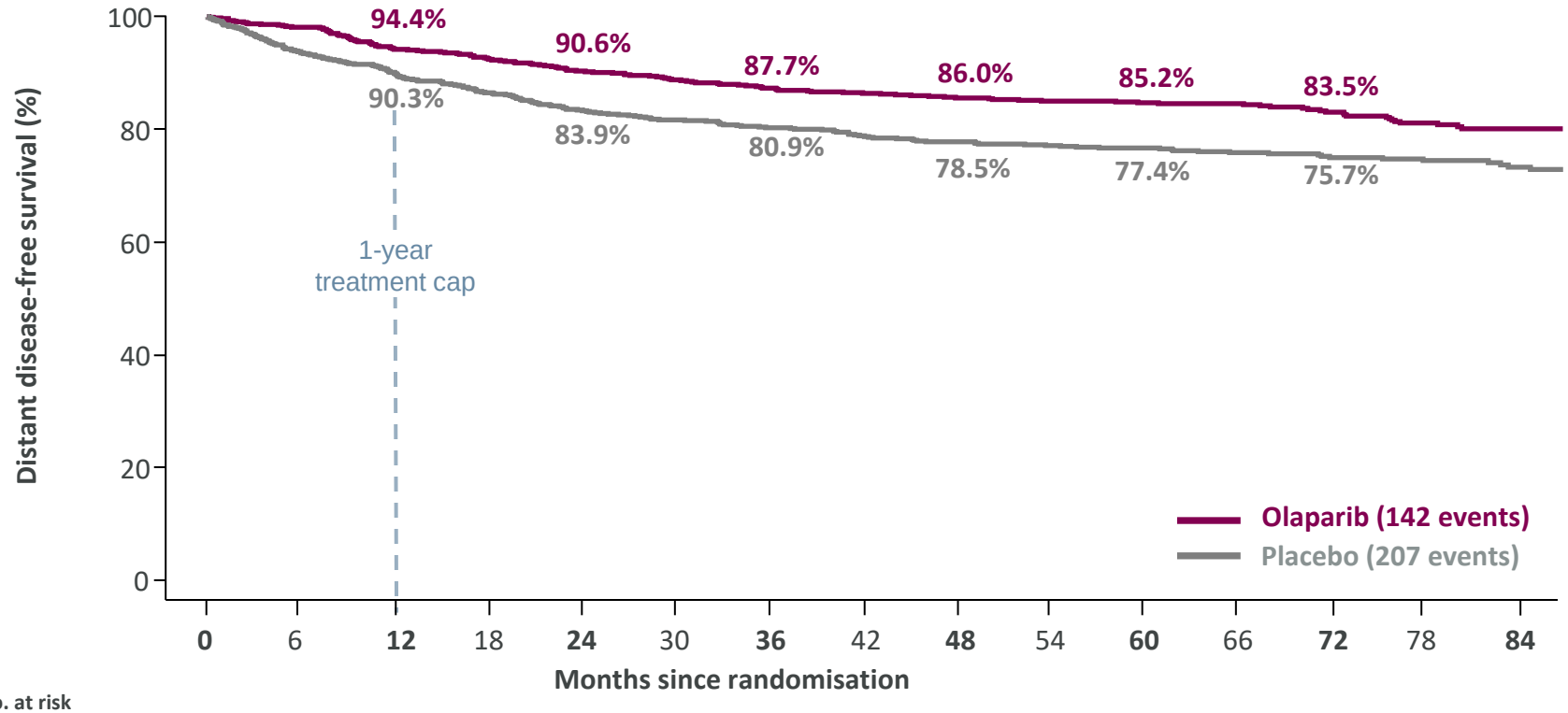
*DCO1 27 March 2020 (at 284 IDFS events, 13% maturity; median follow-up 2.5 years; †Non-proportional hazards; 99.5% CI is shown for the HR for DDFS because p<0.005 was required to indicate statistical significance for this endpoint

Tutt ANJ et al. *N Engl J Med.* 2021; 384:2394-2405.

ABBREVIATIONS

Longer follow-up confirms DDFS benefit of adjuvant olaparib vs placebo with over 7% more patients free of distant recurrence at 6 years

Exploratory analysis: distant disease-free survival (descriptive)



No. at risk								
Olaparib	921	785	718	679	649	588	373	200
Placebo	915	778	698	649	604	534	340	189

DDFS at DCO3

HR 0.65
95% CI, 0.53–0.81

6-year DDFS rate

Olaparib (n=921) **83.5%**

Placebo (n=915) **75.7%**

Difference 7.8%
95% CI, 3.8–11.5

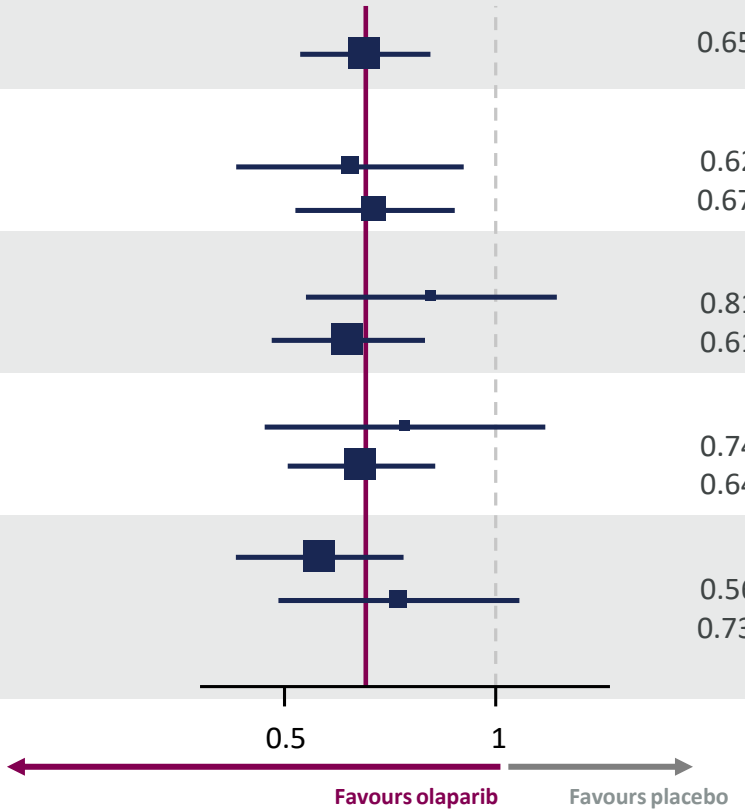
ABBREVIATIONS

DCO3 June 2024; median follow-up 6.1 years.

Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

A consistent benefit was seen across key DDFS subgroups with long term follow-up (DCO3)

Subgroup	Olaparib	Placebo	Stratified hazard ratio for OS (95% CI)	P value for heterogeneity
	No. of patients who died /total no.			
All patients	142 / 921	207 / 915	0.653 (0.526 – 0.807)	NA
Prior chemo				
Adjuvant	45 / 461	72 / 455	0.623 (0.427 - 0.901)	0.73
Neoadjuvant	97 / 460	135 / 460	0.675 (0.518 – 0.874)	
Prior platinum				
Yes	42 / 247	50 / 238	0.812 (0.537 - 1.222)	0.27
No	100 / 674	157 / 677	0.618 (0.480 - 0.793)	
HR status				
HR-positive/HER2-negative	33 / 168	41 / 157	0.745 (0.469 - 1.177)	0.59
TNBC	109 / 751	166 / 758	0.645 (0.505 - 0.820)	
BRCA				
BRCA1	81 / 579	138 / 588	0.563 (0.426 - 0.739)	0.57
BRCA2	45 / 235	55 / 216	0.730 (0.490 – 1.081)	
BRCA1 and *BRCA2*	0 / 2	0 / 3	NC	



DCO3 June 2024; median follow-up 6.1 years.

All subgroup hazard ratio estimates are <1 and all confidence intervals include the ITT population hazard ratio (shown by solid red vertical line as per Cuzick J., Lancet 2005; 365:1308)

ABBREVIATIONS

Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

Fewer patients in the olaparib arm vs. placebo had second primary non-breast cancers

Fewer patients in the olaparib arm had a CNS recurrence vs. the placebo arm

n (%)	Olaparib N=921		Placebo N=915	
	DCO3 June 2024[1]	DCO2 July 2021[2]	DCO3 June 2024[1]	DCO2 July 2021[2]
Number of patients with a first IDFS events*	178 (19.3)	134 (14.5)	258 (28.2)	207 (22.6)
Distant recurrence	106 (11.5)	88 (9.6)	149 (16.3)	136 (14.9)
Distant CNS recurrence	26 (2.8)	24 (2.6)	40 (4.4)	38 (4.2)
Distant excluding CNS recurrence	80 (8.7)	64 (6.9)	109 (11.9)	98 (10.7)
Regional (ipsilateral) recurrence	11 (1.2)	9 (1.0)	22 (2.4)	18 (2.0)
Local (ipsilateral) recurrence	11 (1.2)	9 (1.0)	12 (1.3)	12 (1.3)
Contralateral invasive breast cancer	26 (2.8)	15 (1.6)	36 (3.9)	18 (2.0)
Second primary non-breast malignancies	20 (2.2)	11 (1.2)	37 (4.0)	23 (2.5)
Deaths without a prior IDFS event†	4 (0.4)	2 (0.2)	2 (0.2)	0

*If two recurrence events are reported within 2 months of each other this is referred to as a simultaneous event and will be considered as a single event. In this situation the worst case will be taken as the event 'type' but the date of recurrence will be the earliest date of the two events. †**Deaths in the olaparib arm**: cardiac arrest (n = 1), heart failure with preserved ejection fraction (n = 1), unknown cause (n = 2); **Deaths in the placebo arm**: COVID19 (n = 1), cardiogenic shock (n = 1).

1. Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX. 2. Geyer C, Garber J, Gelber R et al. *Annals of Oncology*. 2022;33(12):1250-1268.

ABBREVIATIONS

The total number of deaths was higher in the placebo arm compared to the olaparib arm, for both DCOs

	Olaparib N=921		Placebo N=915	
n (%)	**DCO3 June 2024[1]**	**DCO2 July 2021[2]**	**DCO3 June 2024[1]**	**DCO2 July 2021[2]**
Total number of deaths*	107 (11.6)	75 (8.1)	143 (15.6)	109 (11.9)
Primary cause of death				
Breast cancer recurrence	94 (10.2)	70 (7.6)	128 (14.0)	103 (11.3)
Other†	13 (1.4)	5 (<1)	15 (1.6)	6 (<1)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

*As reported on the CRF (Death page).
†Other cause of death (including fatal AEs): olaparib: pancreatic carcinoma (n = 1), acute myeloid leukemia (n = 3), cardiovascular (n= 4), multiple organ dysfunction syndrome (n = 1), neutropenic sepsis (n = 1), unknown (n = 3)
placebo: ovarian cancer (n = 2), pancreatic carcinoma (n = 1), pharyngeal carcinoma (n = 1), acute myeloid leukaemia (n = 3), myelodysplastic syndrome (n = 1), pneumonitis (n = 1), cardiovascular (n = 2), superior vena cava occlusion (n = 1), covid-19 (n = 1), unknown (n = 2).

ABBREVIATIONS

1. Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX. 2. Geyer C, Garber J, Gelber R et al. *Annals of Oncology*. 2022;33(12):1250-1268

5

Safety

>70% of patients completed treatment according to protocol without the need for a dose reduction

	Olaparib n=921	Placebo n=915
Completed treatment per protocol, *n (%)*[*‡]	674 (73.2)	715 (78.1)

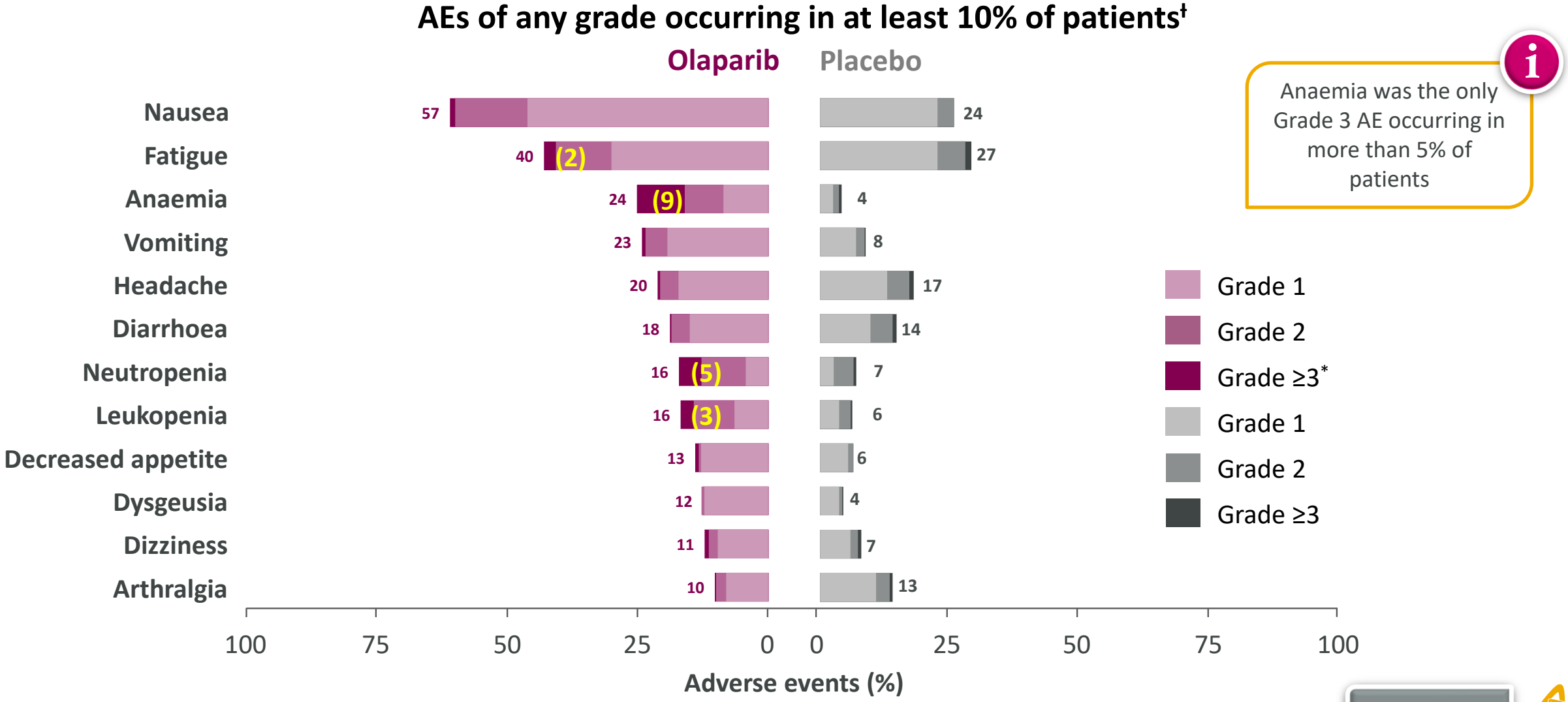
	Olaparib* n=911	Placebo* n=904
Patients with no dose reduction, *n (%)*[ŧ]	683 (75.0)	857 (94.8)
Reason for reduction, *n (%)*[‡]		
Adverse event	222 (24.4)	35 (3.9)
Dosing error	6 (0.7)	10 (1.1)
Administrative reasons	2 (0.2)	1 (0.1)
Other	0 (0.0)	1 (0.1)
Patients with no dose interruption, *n (%)*[ŧ]	392 (43.0)	499 (55.2)
Reason for interruption, *n (%)*[‡]		
Adverse event	330 (36.2)	238 (26.3)
Surgery	226 (24.8)	10 (1.1)
Recurrence of disease	38 (4.2)	78 (8.6)
Others (including dosing error and administrative reasons)	27 (3.0)	40 (4.4)

*Safety analysis set (n=911 in olaparib arm and n=904 in placebo arm). 21 patients who did not received study treatment (n=10 in olarpib arm and n=11 in placebo arm) were excluded from the safety analysis set; ŧDCO1 12 July 2021; ‡Reasons for dose reductions are not mutually exclusive for patients with multiple reductions although are counted only once per category.

1. In House Data. AstraZeneca Pharmaceuticals LP. Data on file. SD-2020-ALL-0091.

ABBREVIATIONS

Adverse events observed were consistent with other trials of olaparib (DCO2)



Anaemia was the only Grade 3 AE occurring in more than 5% of patients

ABBREVIATIONS

**Number presented only where at least 1% have grade 3 AE ;* †DCO2 12 July 2021

Geyer C, Garber J, Gelber R et al. *Annals of Oncology*. 2022;33(12):1250-1268.

No new safety signals were observed with longer term follow-up, and there is no evidence of increased risk of MDS, AML

	Olaparib n=911		Placebo n=904	
AE, *n (%)**	DCO3 June 2024[1]	DCO2 July 2021[2]	DCO3 June 2024[1]	DCO2 July 2021[2]
Any AE[2]	NP	836 (91.8)	NP	758 (83.8)
Serious AE[2]	NP	79 (8.7)	NP	78 (8.6)
AE of special interest at any time*	57 (6.3)	31 (3.4)	84 (9.3)	51 (5.6)
On treatment AESIs†	14 (1.5)	14 (1.5)	28 (3.1)	27 (3.0)
AESI > 30 days after last dose	44 (4.8)	18 (2.0)	57 (6.3)	24 (2.7)
MDS/AML	4 (0.4)	2 (0.2)	6 (0.7)	3 (0.3)
Pneumonitis	9 (1.0)	9 (1.0)	13 (1.4)	12 (1.3)
New primary malignancy Breast Ovary/Fallopian tube Pancreas Other	45 (4.9) 26 (2.9) 5 (<1) 3 (<1) 13 (1.4)	21 (2.3) 14 (1.5) 2 (<1) 0 (0) 6 (<1)	68 (7.5) 36 (4.0) 14 (1.5) 1 (<1) 21 (2.3)	36 (4.0) 16 (1.8) 10 (1.1) 1 (<1) 10 (1.1)
Grade ≥3 AE[2]	NP	221 (24.5)	NP	221 (24.5)
Grade 4 AE‡[2,3]	NP	17 (1.9)	NP	17 (1.9)
AE leading to permanent discontinuation of treatment[2]	NP	98 (10.8)	NP	42 (4.6)
AE leading to death § [2,3]	5 (<1)	2 (<1)[1]	10 (1.1)	4 (<1)[1]

ABBREVIATIONS

Check notes for more information.

1. Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX. 2. Geyer C, Garber J, Gelber R et al. *Annals of Oncology*. 2022;33(12):1250-1268. 3. Tutt ANJ et al. *N Engl J Med.* 2021; 384:2394-2405.

Blood transfusions were infrequently required*

Majority of patients who required blood transfusion only had one transfusion

n (%)	Olaparib n=921	Placebo n=915
Patients with at least one blood transfusion	53 (5.8)	8 (0.9)
With ≥ grade 3 anaemia on treatment	42 (4.6)	2 (0.2)
With < grade 3 anaemia on treatment	9 (1.0)	2 (0.2)
No anaemia reported on treatment	2 (0.2)	4 (0.4)
Number of patients with only 1 transfusion	37 (4.1)	6 (0.7)
Number of patients with 2 transfusions	13 (1.4)	2 (0.2)
Number of patients with 3 or more transfusions	3 (0.3)	0 (0.0)

*DCO1 27 March 2020

Tutt ANJ et al. Supplementary Appendix *N Engl J Med.* 2021;384:2394-2405.

ABBREVIATIONS

New cancers of special interest were similar between the 2 arms, except for ovarian/fallopian tube that had a higher incidence on the placebo group (DCO3)

n (%)	Olaparib n=911	Placebo n=904
Bilateral mastectomy prior to randomization	339 (36.8)	321 (35.1)
Bilateral mastectomy post randomization	143 (15.5)	163 (17.8)
Patients with contralateral invasive breast cancer*	**34**	**42**
Patients with contralateral non-invasive breast cancer	**3**	**4**
Bilateral salpingectomy or BSO prior to randomization†	186 (20.2)	168 (18.4)
Bilateral salpingectomy or BSO post randomization‡	239 (26.0)	249 (27.2)
Patients with new primary ovarian or fallopian tube cancer §	**5**	**14**

DCO3 June 2024; median follow-up 6.1 years.

*1 patient in the olaparib arm and 1 patient in the placebo arm had BSO prior to new primary ovarian cancer

†Salpingectomy only recorded; **olaparib** (n = 1), **placebo** (n = 2); oophorectomy only recorded **olaparib** (n = 22), **placebo** (n = 13).

‡Salpingectomy only recorded; **olaparib** (n = 2), **placebo** (n = 4); oophorectomy only recorded **olaparib** (n = 14), **placebo** (n = 13).

§1 patient in the olaparib arm and 1 patient in the placebo arm had BSO prior to new primary ovarian cancer

ABBREVIATIONS

Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

The number of reported pregnancies and outcomes were similar between the 2 arms (DCO3)

	Olaparib n=921	Placebo n=915
Number of patients (%)	41 (4.5%)	40 (4.4%)
Number of pregnancies*	51	51
Pregnancy outcomes		
Full Term	32	39
Premature Birth	2	3
Spontaneous Miscarriage	8	6
Termination	6	3
Missing	3	0

DCO3 June 2024; median follow-up 6.1 years.

*In the olaparib arm 8 patients had 2 pregnancies and 1 patient had 3 pregnancies. In the placebo arm 7 patients had 2 pregnancies and 1 patient had 5 pregnancies.

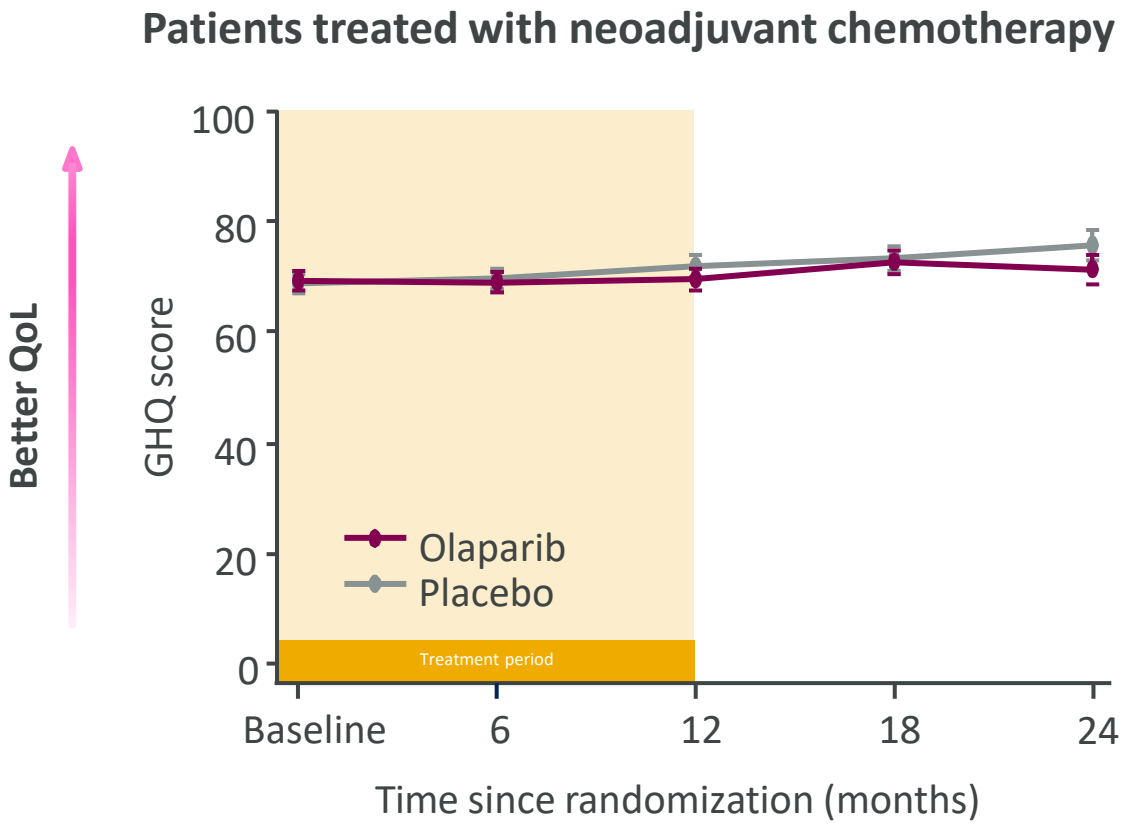
Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

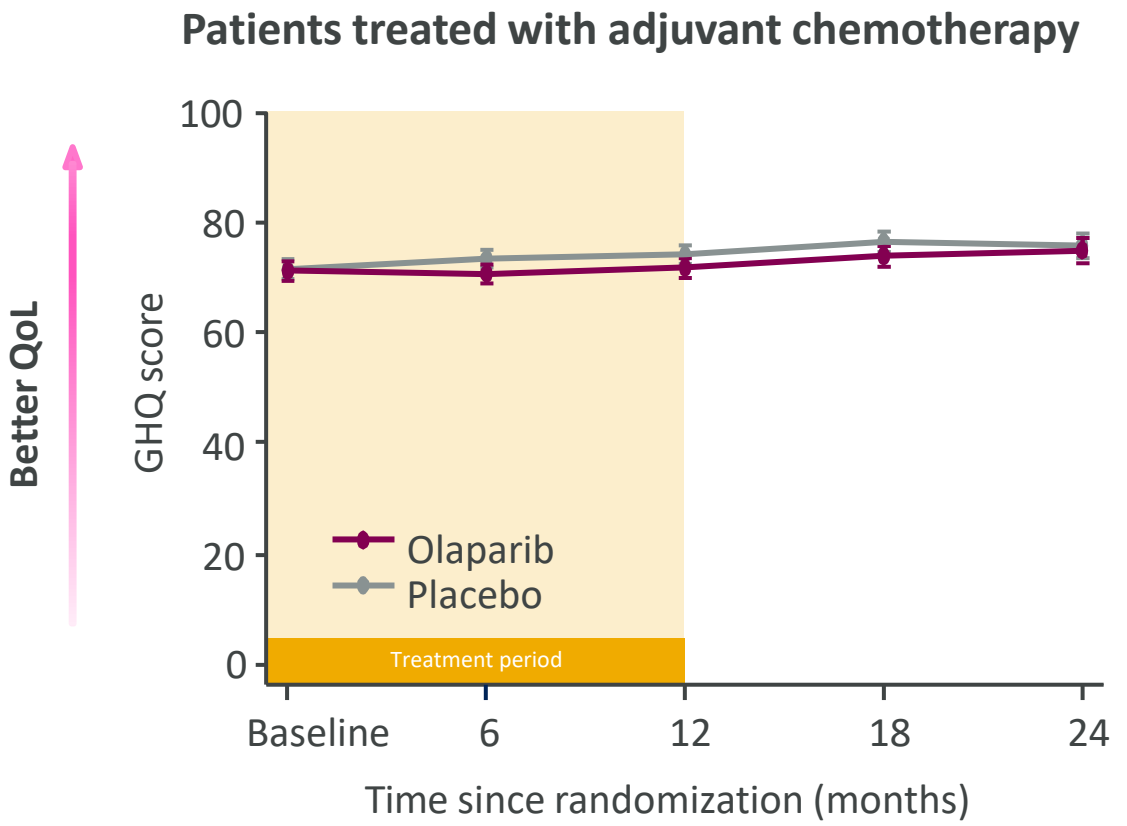
ABBREVIATIONS

6

HRQoL

One year of adjuvant olaparib maintained global health status HRQoL vs. placebo





1,533 patients were analysed for GHQ; 744 were in the neoadjuvant chemotherapy group and 791 were in the adjuvant chemotherapy group.
*Global Health Quality (GHQ) score ranges from 0 to 100, higher score indicates better QoL. Adjusted least-square mean responses and 95% CI for time points other than baseline are obtained from mixed model for repeated measures analysis of the GHQ score. The model includes treatment, time and treatment by time interaction, corresponding baseline score, and the baseline score by time interaction.

DCO1 27 March 2020

1. Tutt ANJ et al. Supplementary Appendix *N Engl J Med.* 2021384:2394-2405. 2. Ganz PA, et al. Presented at SABCS 2021. 7–10 December. San Antonio, TX.

ABBREVIATIONS

7

Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for breast cancer recommends addition of olaparib following adjuvant chemotherapy for certain high-risk, HER2-negative, BC patients with gBRCAm

Olaparib is listed as a **preferred regimen option**[a,b] for HER2-negative breast cancer in certain high-risk patients with germline *BRCA1/2* mutations[1]

- Olaparib is recommended as an option for 1 year after neoadjuvant or adjuvant chemotherapy.[a]
- This recommendation is for select TNBC (category 1) and select HR-positive disease (category 2A).[a,b]

[a]Consider addition of adjuvant olaparib for 1 year after adjuvant chemotherapy for those with germline BRCA1/2 mutations and:
- TNBC, if 1) ≥pT2 or ≥pN1 disease after adjuvant chemotherapy, or 2) *residual disease after preoperative chemotherapy (category 2A)*
- HR-positive, HER2-negative tumors, if 1) ≥4 positive lymph nodes after adjuvant chemotherapy (category 2A) , or 2) residual disease after preoperative therapy and clinical stage, pathological stage, estrogen receptor status, and tumor grade (CPS + EG) score ≥3. (category 2A). Adjuvant olaparib can be used concurrently with endocrine therapy.

[b]Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

ABBREVIATIONS

ASCO® Clinical Practice Guidelines: rapid recommendation update to include olaparib as adjuvant therapy on the Management of Hereditary Breast Cancer

Recommendation: For patients with early-stage, HER2-negative breast cancer with high risk of recurrence and germline *BRCA1* or *BRCA2* pathogenic or likely pathogenic variants, one year of **adjuvant olaparib should be offered** after completion of (neo)adjuvant chemotherapy and local treatment, including radiation[1]

- For those who had surgery first, adjuvant olaparib is recommended for patients with:
  - TNBC: tumor size> 2 cm, or any involved axillary nodes.
  - HR+ disease: at least four involved axillary lymph nodes.
- For patients who had neoadjuvant chemotherapy, adjuvant olaparib is recommended for patients with:
  - TNBC: any residual cancer;
  - HR+ disease: residual disease and an estrogen receptor status and tumor grade (CSP+EG) score ≥ 3.

ABBREVIATIONS

Tung NM et al. *J Clin Oncol*. 2021;39:2959-2961.

St Gallen Consensus Guidelines endorse adjuvant olaparib in women with Stage 2 or 3, HER2-negative breast cancer

Over **93%** of 74 international experts **strongly endorsed adjuvant olaparib** for women with Stage II or III, HER2-negative breast cancer meeting the eligibility criteria of the OlympiA study.

64% strongly endorsed olaparib therapy, irrespective of ER status or prior treatment with platinum-based chemotherapy.

95% of panel voters recommended genetic testing of patients meeting the OlympiA study entry criteria.

ABBREVIATIONS

Burstein HJ et al. *Ann. Oncol*. 2021;32(10):1216-1235.

OlympiA Conclusions

- The OlympiA trial is the first to report the clinical benefits of a PARP inhibitor (olaparib) as an adjuvant treatment in patients with gBRCAm, HER2-negative high risk eBC
- With ~9% more patients recurrence free at 3 years, 1 year adjuvant olaparib significantly reduced the risk of recurrence or death by 42% vs. placebo
- Adjuvant olaparib resulted in patients living longer, with a 32% reduction in risk of death vs placeob. 3.4% more patients treated with olaparib were alive at 4 years vs. placebo
- Consistent with previous studies, the safety profile of olaparib was generally manageable, with the majority of AEs being Grade 1 or 2
- Test for gBRCAm at diagnosis to inform treatment decisions and maximise long term outcomes

ABBREVIATIONS