AstraZeneca
What science can do

Investor science conference call: European Society for Medical Oncology (ESMO) Congress 2019

Conference call for investors and analysts

30 September 2019

Forward-looking statements

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Speakers

Pascal Soriot
Executive Director and
Chief Executive Officer

Dave Fredrickson
Executive Vice President,
Oncology Business Unit

Dr. Isabelle Ray-Coquard
Primary investigator of the
Lynparza Phase III PAOLA-1
trial

José Baselga
Executive Vice President,
Oncology R&D

Agenda

Introduction

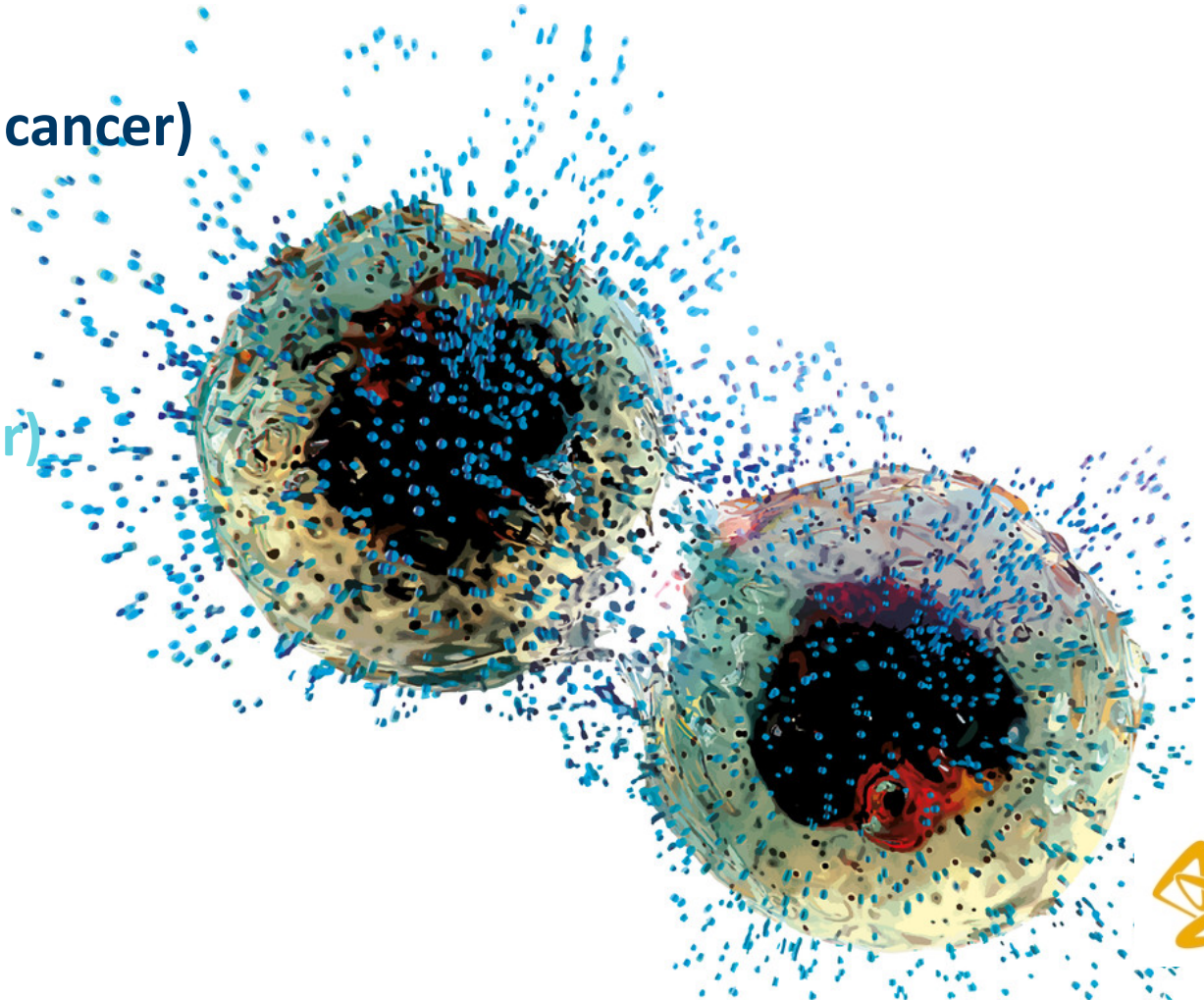
***Lynparza*'s Phase III PAOLA-1 trial (ovarian cancer)**

Other Phase III data at ESMO 2019

-*Lynparza*'s PROfound trial (prostate cancer)

-*Tagrisso*'s FLAURA trial (lung cancer)

Closing and Q&A



Oncology: strategy

A leading, diversified oncology business

Lung cancer	Lung cancer	Multiple cancers	Multiple cancers	Haematology
TAGRISSO® osimertinib	IMFINZI™ durvalumab Injection for Intravenous Use 50 mg/mL	Lynparza™ olaparib	**trastuzumab deruxtecan**	CALQUENCE® (acalabrutinib) 100 mg capsules
• Stage IV NSCLC[1] T790Mm[2] / EGFRm[3] • Next: adjuvant, Stage III	• Unresectable, Stage III NSCLC • Next: early/advanced stages in several cancers	• Ovarian, breast cancers • MRK collaboration • Next: pancreatic, prostate cancers	• DS[4] collaboration • Next: HER2+[5] breast, gastric cancers; HER2-low cancers	• First medicine in haematology • MCL[6] launched • CLL[7] data started • Next: combinations

‘What’s next’: rich early to mid-stage pipeline, including combinations

1. Non-small cell lung cancer 2. Substitution of threonine (T) with methionine (M) at position 790 of exon 20 mutation 3. Epidermal growth factor receptor mutation 4. Daiichi Sankyo 5. Human epidermal growth factor receptor 2 positive
6. Mantle cell lymphoma 7. Chronic lymphocytic leukaemia.

AstraZeneca redefines cancer treatment at ESMO 2019

>60 abstracts accepted, five presidential and seven oral presentations

Key Phase III presentations

- ***Tagrisso***

FLAURA OS[1] - EGFRm NSCLC

- ***Lynparza***

PAOLA-1 - ovarian cancer
PROfound - prostate cancer

- ***Imfinzi***

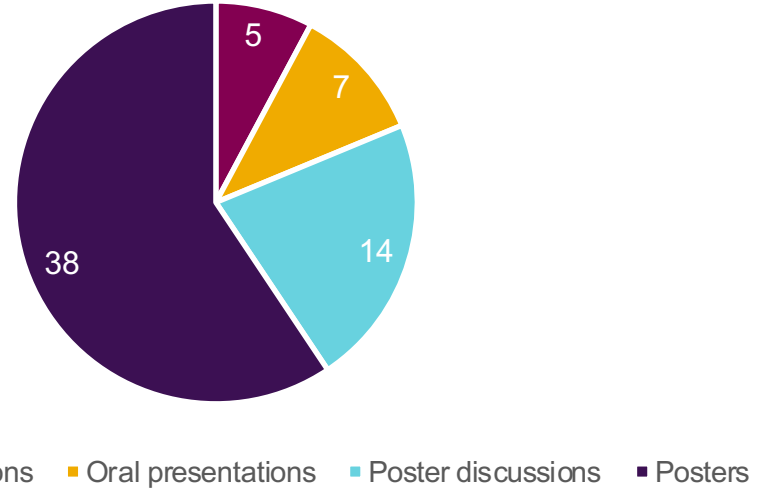
CASPIAN - SCLC[2]

- ***Faslodex* OS**

MONARCH2 - breast cancer
MONALEESA-3 - breast cancer

ESMO abstracts

- Over 60 abstracts, including **five presidential** and **seven oral presentations**
- Five late-breaking abstracts
- Externally sponsored c. 40% of total



1. Overall survival 2. Small cell lung cancer.

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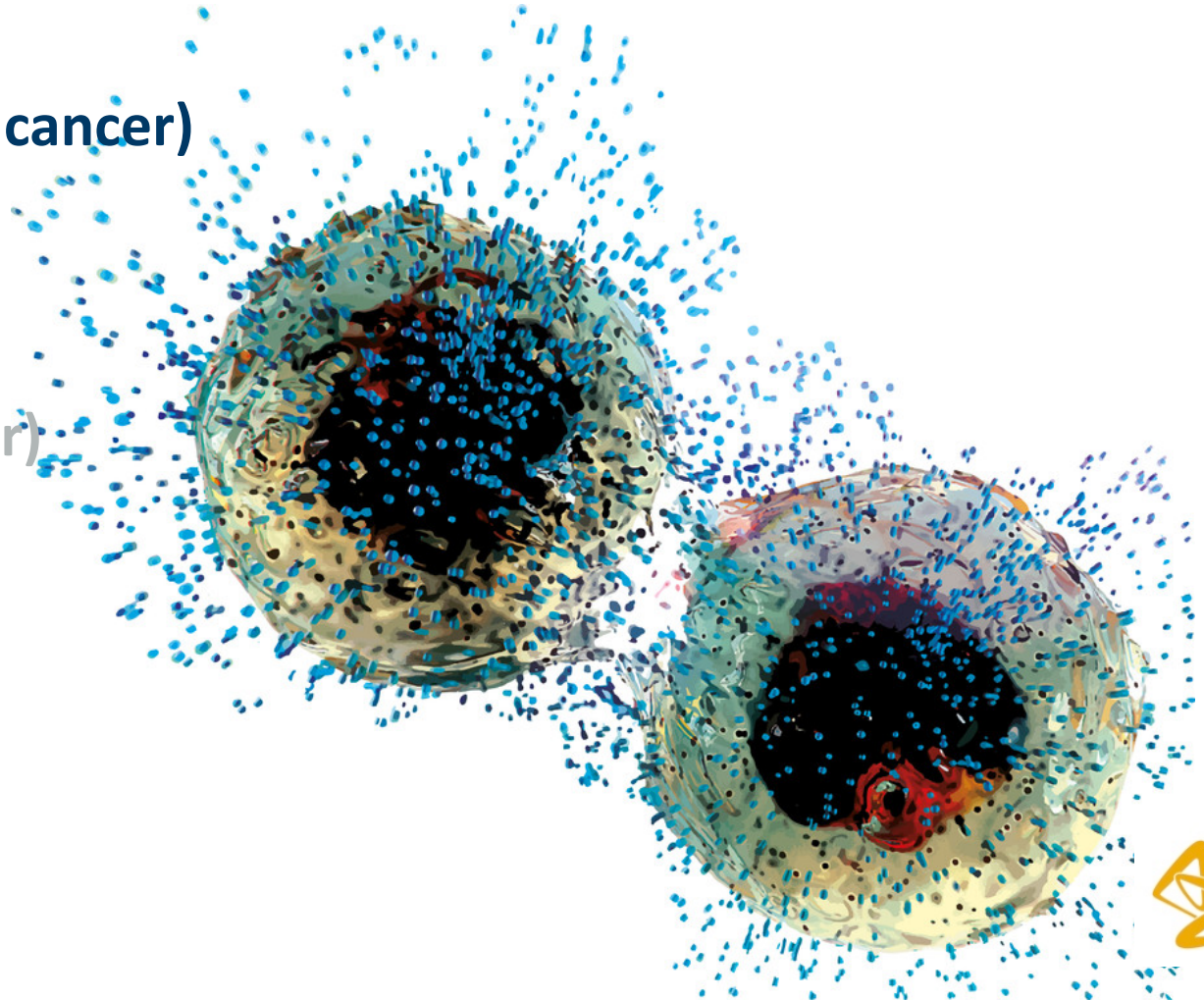
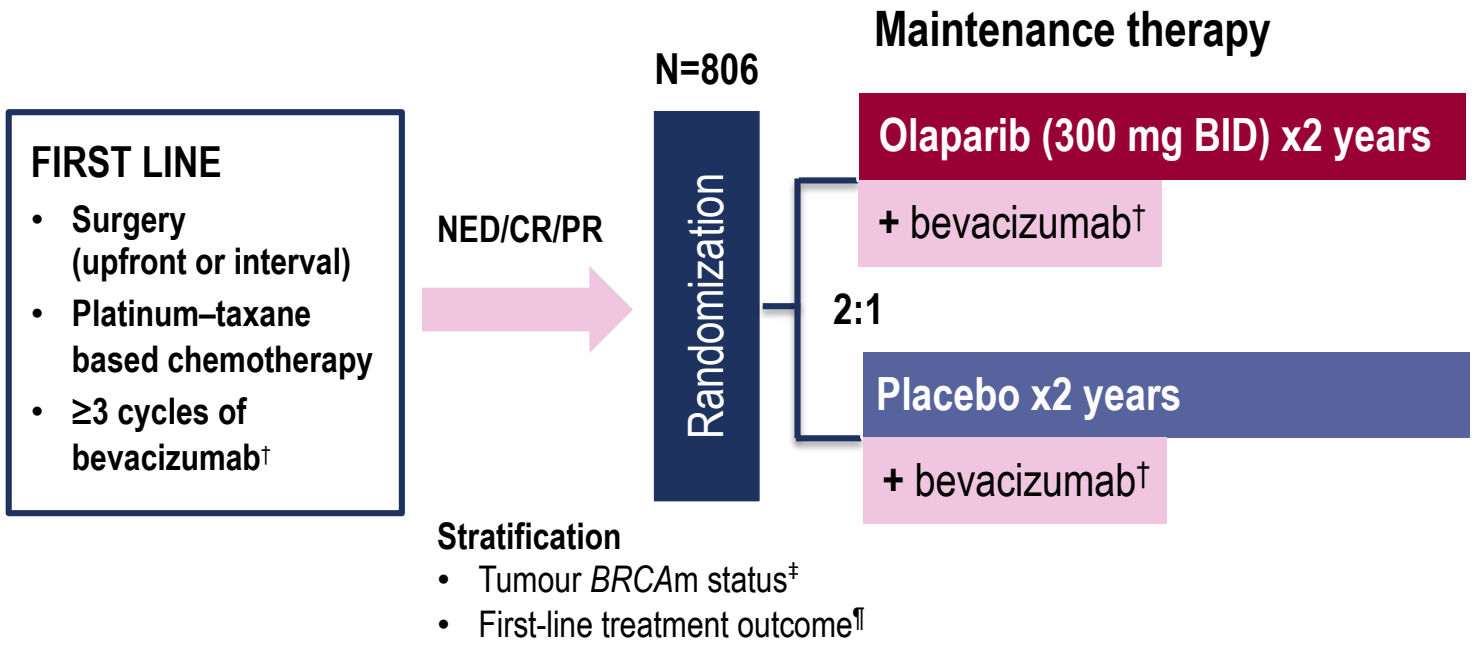


Lynparza's Phase III PAOLA-1 trial | 1

Study design

Newly diagnosed FIGO stage III–IV high-grade serous/endometrioid ovarian, fallopian tube or primary peritoneal cancer*



*Patients with other epithelial non-mucinous ovarian cancer were eligible if they had a germline *BRCA1* and/or *BRCA2* mutation
†Bevacizumab: 15 mg/kg, every 3 weeks for a total of 15 months, including when administered with chemotherapy; ‡By central labs; ¶According to timing of surgery and NED/CR/PR
BID, twice daily; *BRCA*m, *BRCA1* and/or *BRCA2* mutation; CR, complete response; NED, no evidence of disease; PR, partial response

Lynparza's Phase III PAOLA-1 trial | 2

Patient disposition

		Olaparib + bevacizumab	Placebo + bevacizumab
Randomized, n		537	269
Treated, n (%)		535 (99.6)	267 (99.3)
Discontinued study treatment, n (%)		331 (62)	194 (73)
	Disease progression per RECIST	182 (34)	155 (58)
	Disease progression non-RECIST	14 (3)	13 (5)
	TEAE	109 (20)	13 (5)
	Patient decision	17 (3)	10 (4)
	Death	1 (<1)	3 (1)
	Other*	8 (1)	0
Median duration of treatment, months (range)	Olaparib/placebo	17.3 (0.03–33.0)	15.6 (0.07–26.2)
	Bevacizumab	11.0 (0.69–21.4)	10.6 (0.69–17.1)
Median duration of follow-up, months		24.0	22.7

*Other includes lost to follow up, surgery, new comorbidities and other

TEAE, treatment-emergent adverse event

Lynparza's Phase III PAOLA-1 trial | 3

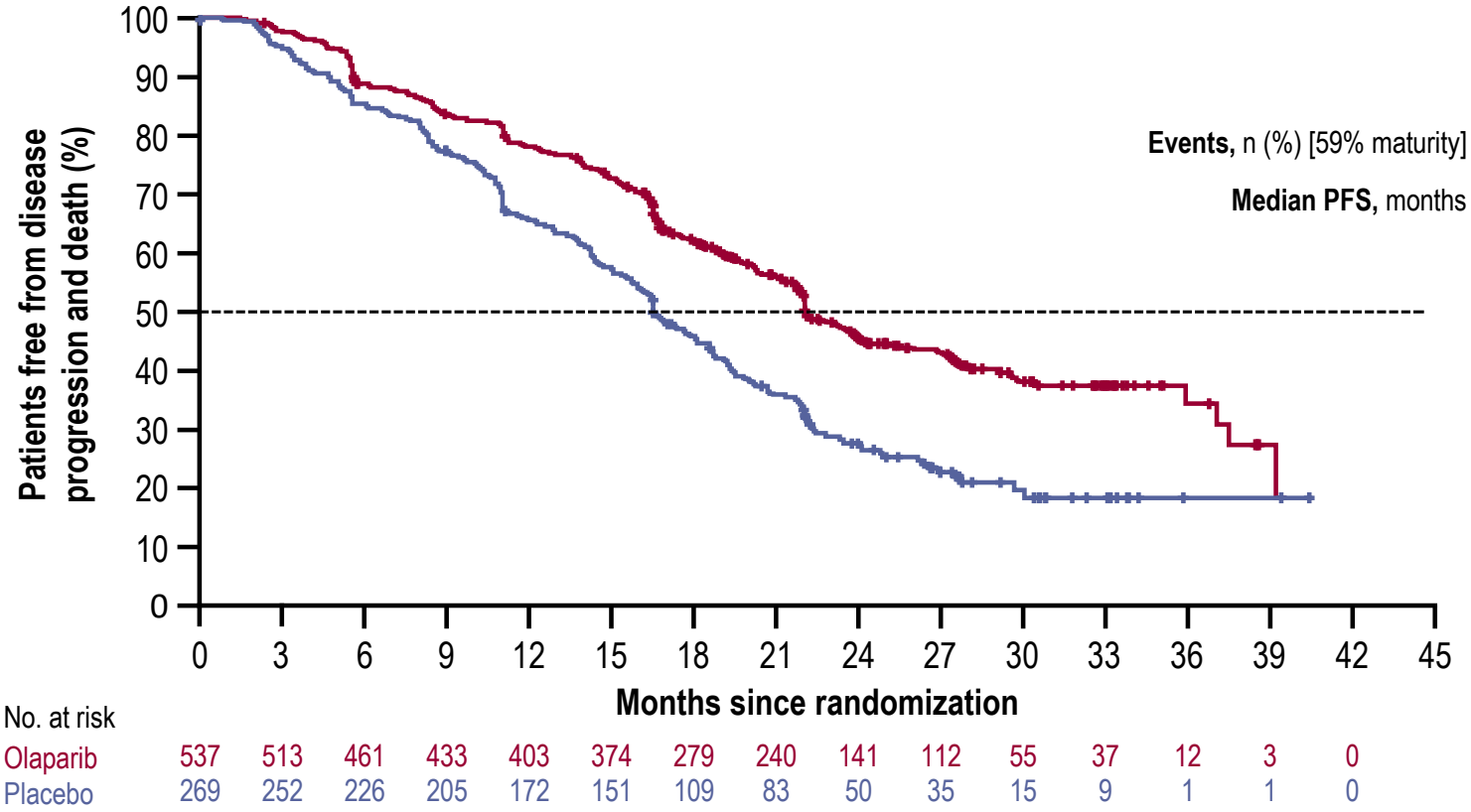
Summary of AEs

	Olaparib + bevacizumab (N=535)	Placebo + bevacizumab (N=267)
All grade TEAEs, n (%)	531 (99)	256 (96)
Grade ≥3 TEAEs, n (%)	303 (57)	136 (51)
SAEs, n (%)	167 (31)	83 (31)
Deaths, n (%)	1 (<1)	4 (1)
Dose interruptions due to AEs, n (%)	291 (54)	65 (24)
Dose reductions due to AEs, n (%)	220 (41)	20 (7)
Discontinuations due to AEs, n (%)	109 (20)	15 (6)

Dose interruptions, reductions and discontinuations reported are for olaparib and placebo
SAE, serious adverse event

Lynparza's Phase III PAOLA-1 trial | 4

PFS by investigator assessment: ITT population



	Olaparib + bevacizumab (N=537)	Placebo + bevacizumab (N=269)
Events, n (%) [59% maturity]	280 (52)	194 (72)
Median PFS, months	**22.1**	**16.6**

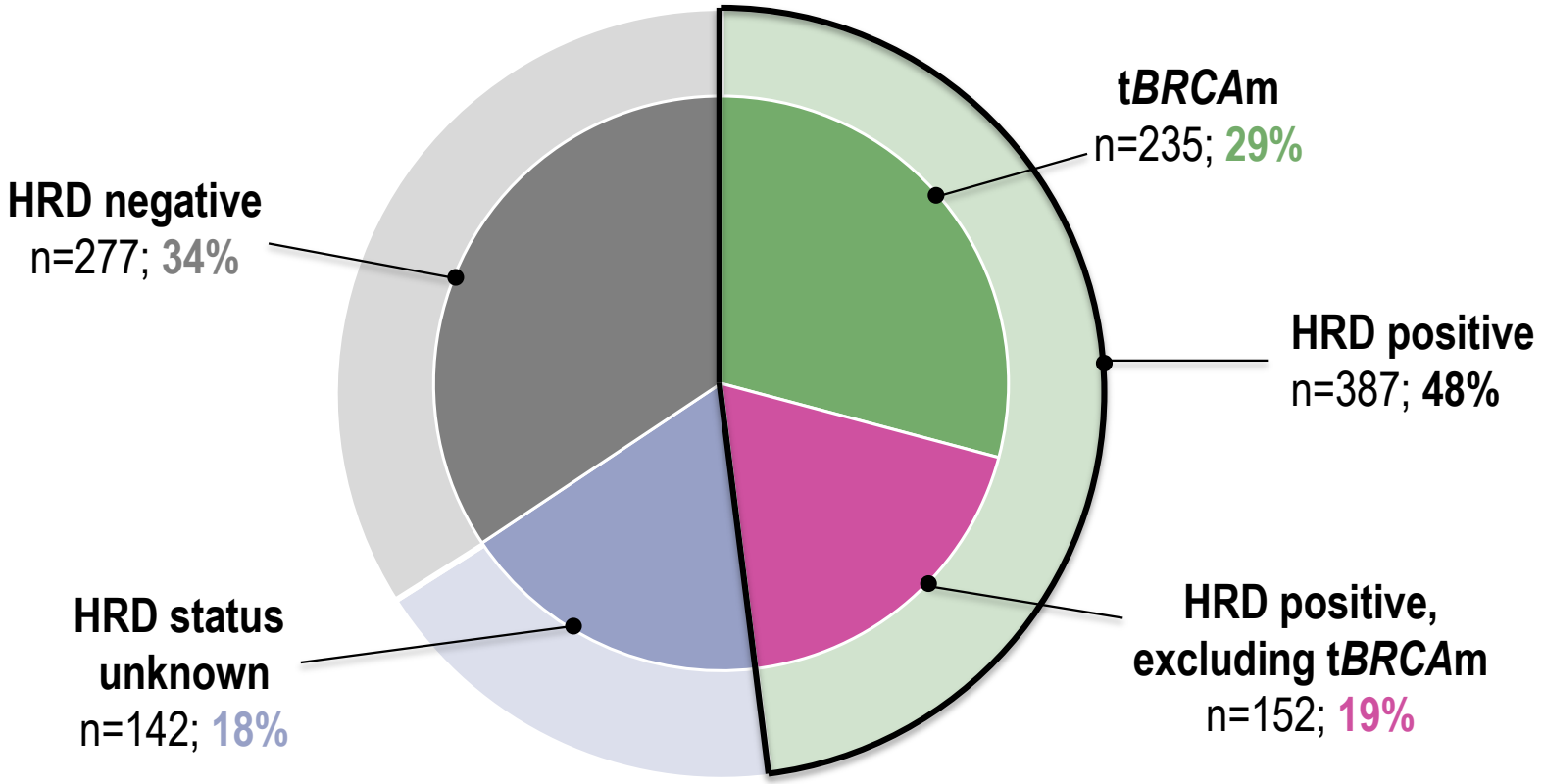
HR 0.59 (95% CI 0.49–0.72; *P*<0.0001)

Median time from first cycle of chemotherapy to randomization = 7 months

ITT, intent-to-treat population

Lynparza's Phase III PAOLA-1 trial | 5

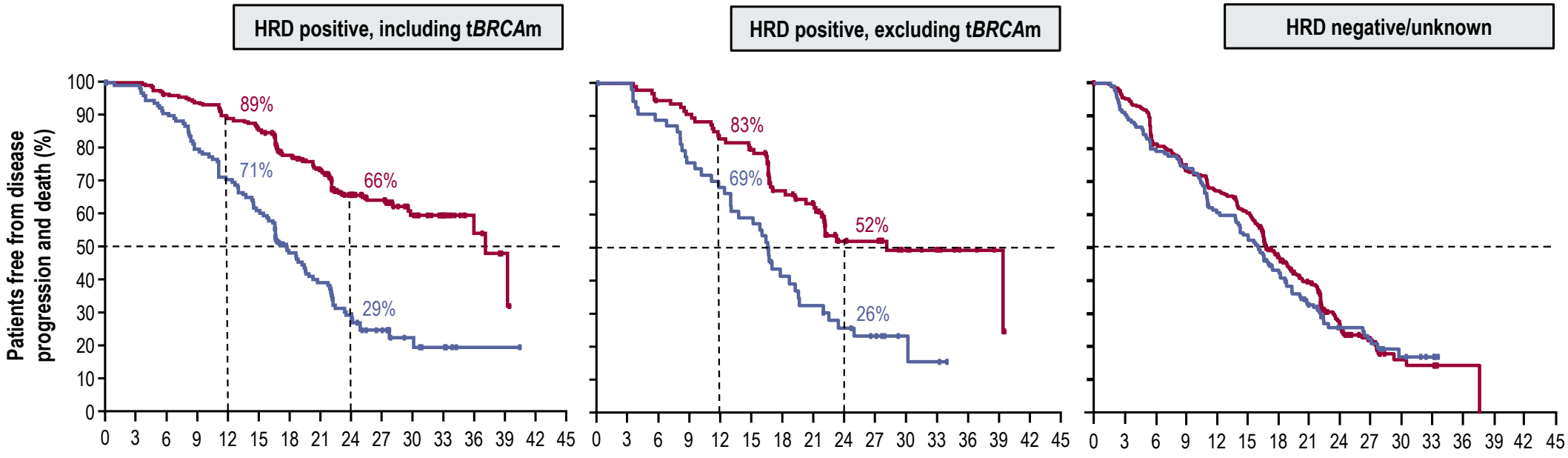
Biomarker subgroups in PAOLA-1/ENGOT-ov25



HRD positive is either tumour *BRCA* mutation and/or HRD score ≥42 by Myriad MyChoice® HRD Plus
Reasons for HRD status unknown: 4.2% missing; 2.1% fail; 11.3% inconclusive

Lynparza's Phase III PAOLA-1 trial | 6

PFS by HRD status



	Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
Events, n (%)	87 (34)	92 (70)
Median PFS, months	**37.2***	**17.7**
	HR 0.33 (95% CI 0.25–0.45)	

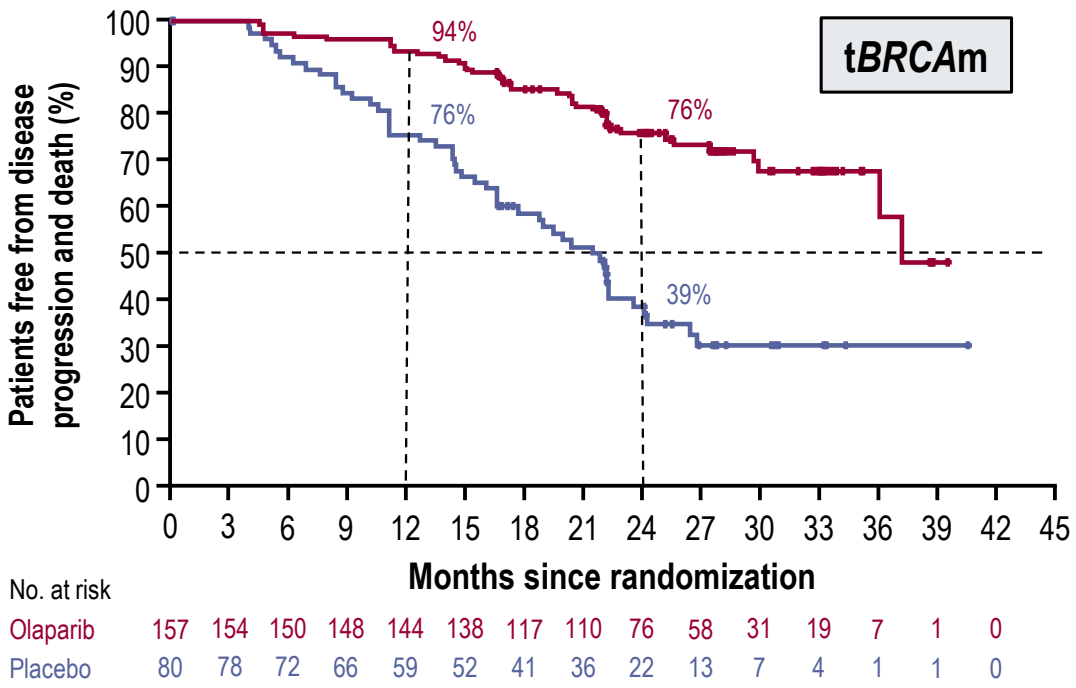
	Olaparib + bevacizumab (N=97)	Placebo + bevacizumab (N=55)
	43 (44)	40 (73)
	28.1*	**16.6**
	HR 0.43 (95% CI 0.28–0.66)	

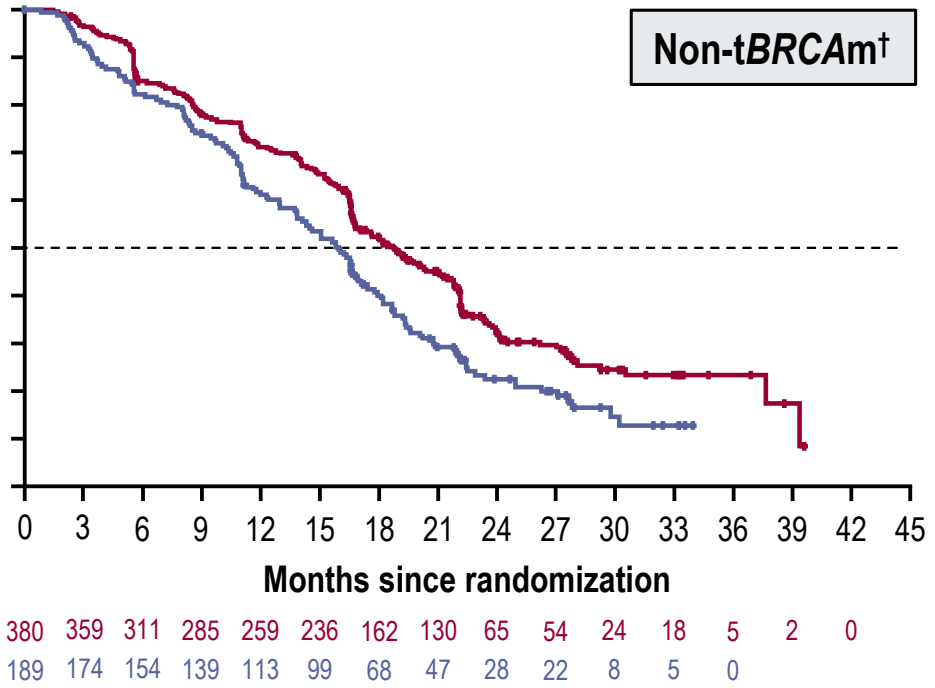
	Olaparib + bevacizumab (N=282)	Placebo + bevacizumab (N=137)
	193 (68)	102 (74)
	16.9	**16.0**
	HR 0.92 (95% CI 0.72–1.17)	

The percentages of patients progression-free at 12 months and 24 months have been calculated based on Kaplan-Meier estimates. HRD positive is an HRD score ≥42. *This median is unstable due to a lack of events – less than 50% maturity

Lynparza's Phase III PAOLA-1 trial | 7

PFS by t*BRCA* mutation status





No. at risk															
Olaparib	157	154	150	148	144	138	117	110	76	58	31	19	7	1	0
Placebo	80	78	72	66	59	52	41	36	22	13	7	4	1	1	0

No. at risk															
Olaparib	380	359	311	285	259	236	162	130	65	54	24	18	5	2	0
Placebo	189	174	154	139	113	99	68	47	28	22	8	5	0		

	Olaparib + bevacizumab (N=157)	Placebo + bevacizumab (N=80)
Events, n (%)	41 (26)	49 (61)
Median PFS, months	**37.2***	**21.7**
	HR 0.31 (95% CI 0.20–0.47)	

	Olaparib + bevacizumab (N=380)	Placebo + bevacizumab (N=189)
	239 (63)	145 (77)
	18.9	**16.0**
	HR 0.71 (95% CI 0.58–0.88)	

The percentages of patients progression-free at 12 months and 24 months have been calculated based on Kaplan-Meier estimates. *This median is unstable due to a lack of events – less than 50% maturity; †Includes t*BRCA* unknown

Lynparza's Phase III PAOLA-1 trial | 8

Conclusions

- PAOLA-1/ENGOT-ov25 included a broad, front-line population of advanced ovarian cancer patients which was not restricted by surgical outcome or *BRCA* mutation status
- PAOLA-1/ENGOT-ov25 met its primary objective, demonstrating a statistically significant improvement in PFS in the ITT population when olaparib compared with placebo was added to first-line standard-of-care bevacizumab maintenance treatment
- Prespecified subgroup analyses showed that patients with t*BRCA* mutations and patients with a positive HRD status had the greatest PFS benefits
  - The results reveal a patient population beyond t*BRCA*m patients, who are HRD positive, that experiences substantial benefit from maintenance treatment with olaparib and bevacizumab
- The safety profile of olaparib in combination with bevacizumab was generally consistent with previous trials of each drug and the addition of olaparib did not impact on bevacizumab tolerability and HRQoL

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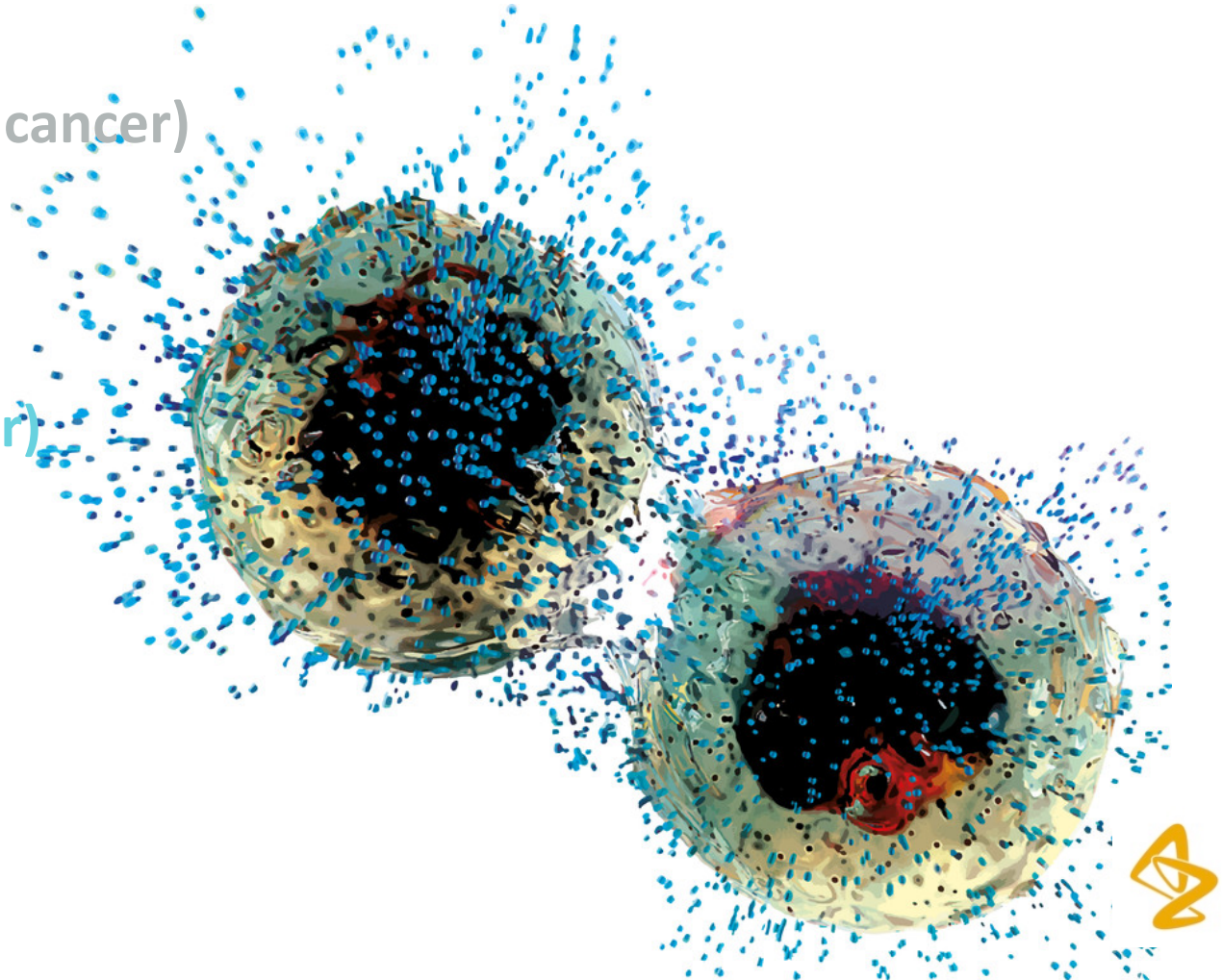
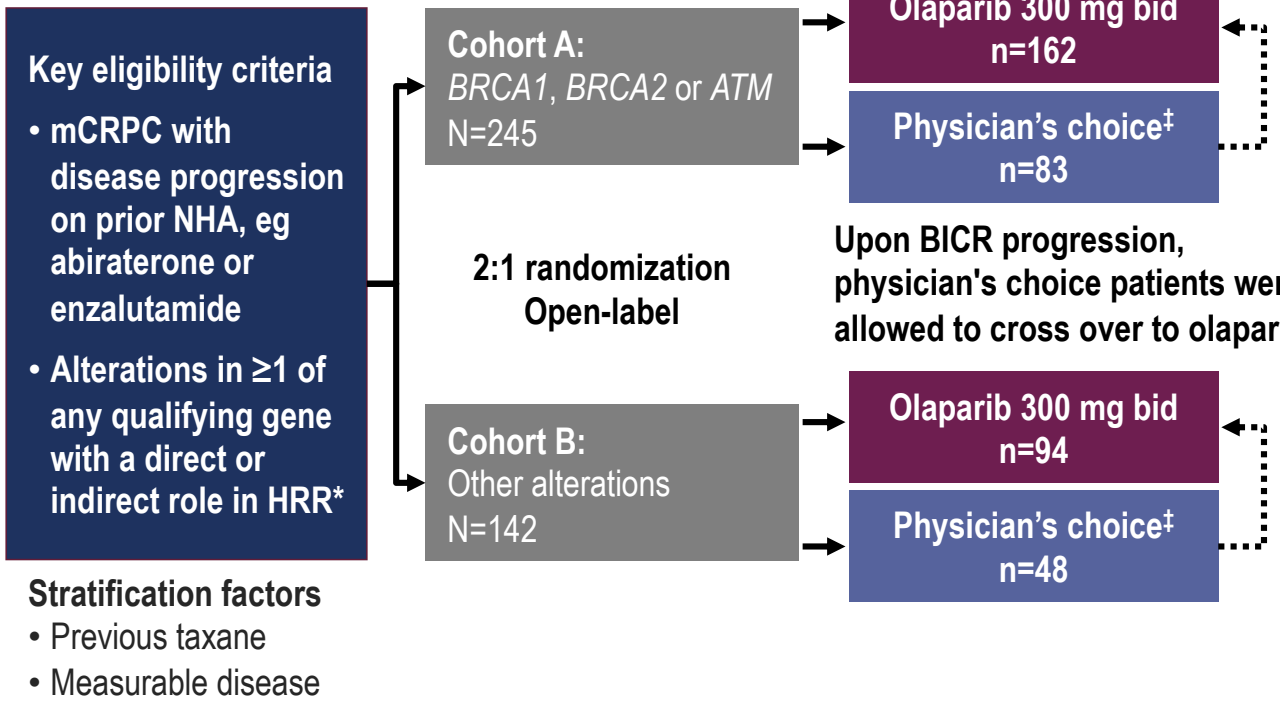


Lynparza's Phase III PROfound trial | 1

STUDY DESIGN



Primary Endpoint

Radiographic progression-free survival (rPFS) in Cohort A (RECIST 1.1 & PCWG3 by BICR)

Key Secondary Endpoints

- rPFS in Cohorts A+B
- Confirmed radiographic objective response rate (ORR) in Cohort A
- Time to pain progression (TTPP) in Cohort A
- Overall survival (OS) in Cohort A

*An investigational Clinical Trial Assay, based on the FoundationOne® CDx next-generation sequencing test, and developed in partnership with Foundation Medicine Inc, was used to prospectively select patients harboring alterations in the following genes in their tumor tissue: *BRCA1*, *BRCA2*, *ATM*, *BARD1*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *PPP2R2A*, *RAD51B*, *RAD51C*, *RAD51D* or *RAD54L*

‡Physician's choice of either enzalutamide (160 mg qd) or abiraterone (1000 mg qd plus prednisone [5 mg bid])
BICR, blinded independent central review

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Lynparza's Phase III PROfound trial | 2

SAFETY SUMMARY IN THE OVERALL POPULATION (COHORTS A+B)

Median treatment duration: Olaparib, 7.4 months; Physician's choice 3.9 months

	Olaparib (N=256)	Physician's choice (N=130)
Any AE, n (%)	244 (95.3)	114 (87.7)
Any AE of CTCAE grade 3 or higher, n (%)	130 (50.8)	49 (37.7)
Dose reduction due to AE, n (%)	57 (22.3)	5 (3.8)
Discontinuation due to AE, n (%)	42 (16.4)	11 (8.5)
Death due to AE, n (%)	10 (3.9)	5 (3.8)
Reported to be related to study treatment	1 (0.4)	1 (0.8)

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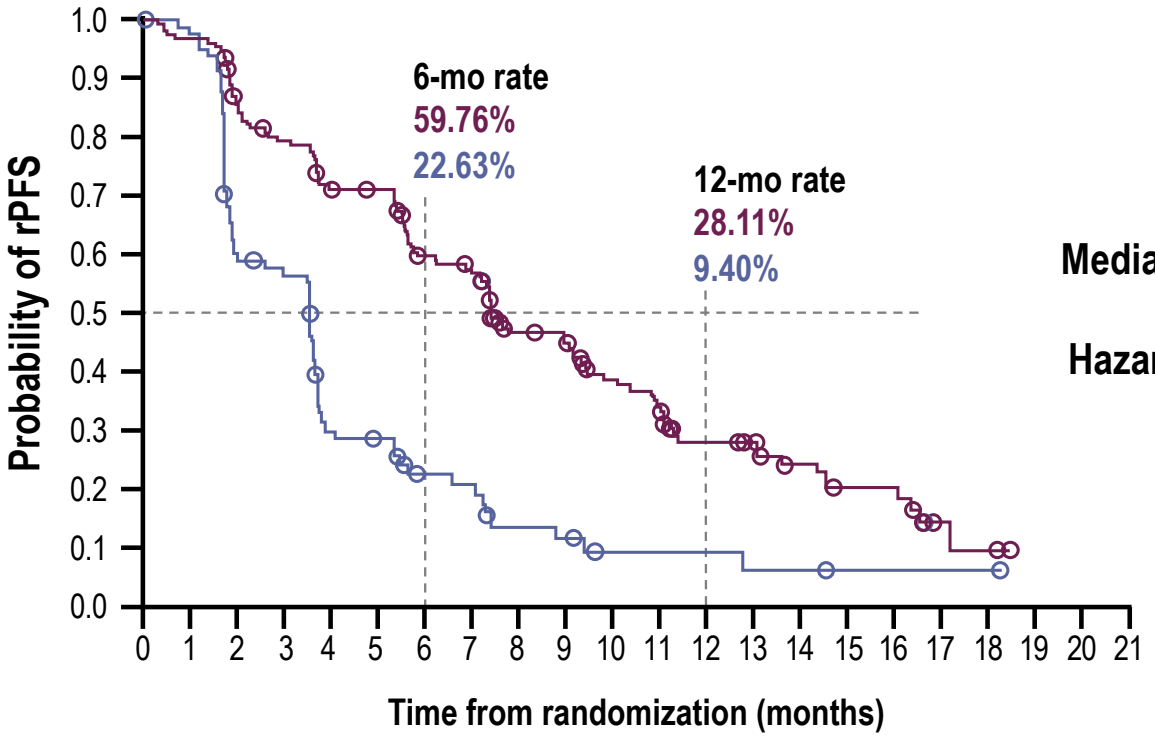
AEs are reported irrespective of attribution, unless otherwise stated

Lynparza's Phase III PROfound trial | 3

Primary endpoint

rPFS BY BICR IN PATIENTS WITH ALTERATIONS IN *BRCA1*, *BRCA2*, OR *ATM* (COHORT A)



	Olaparib (N=162)	Physician's choice (N=83)
Events (%)	106 (65.4)	68 (81.9)
Median PFS (months)	7.39	3.55
Hazard ratio (95% CI)	0.34 (0.25, 0.47) *P*<0.0001	

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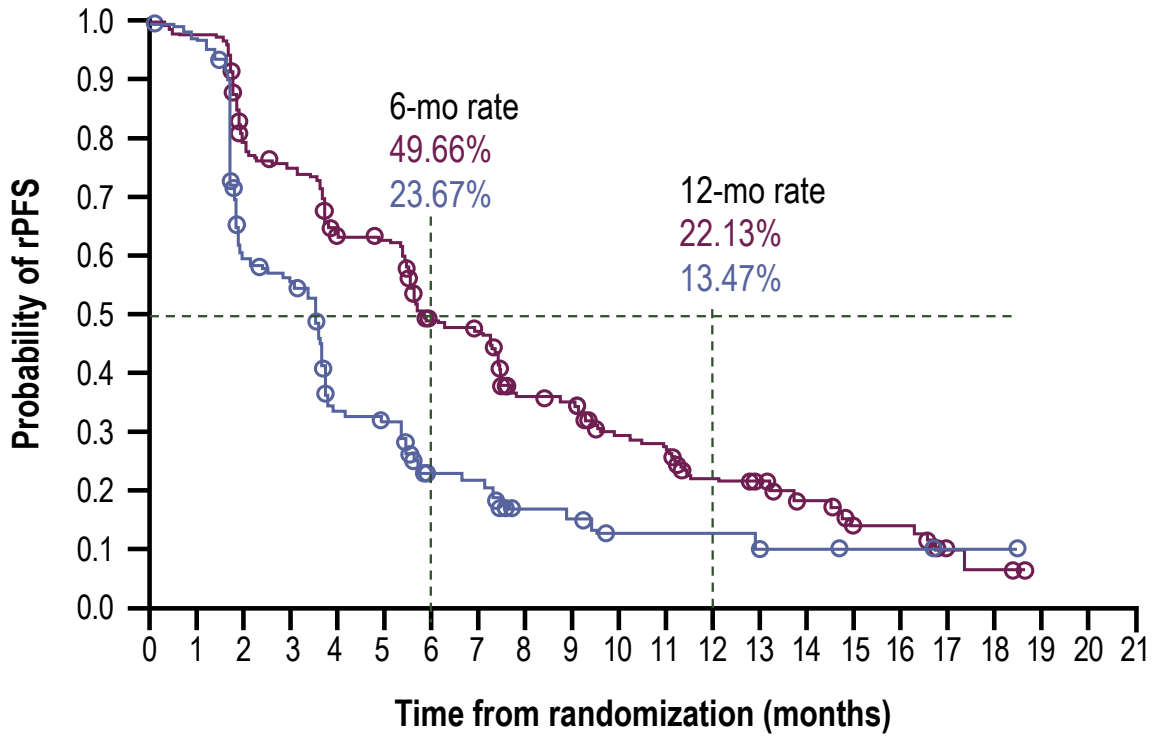
Prespecified sensitivity analysis based on investigator assessment: Hazard ratio 0.24 (95% CI 0.17, 0.34); *P*<0.0001

Lynparza's Phase III PROfound trial | 4

Key secondary endpoint

rPFS BY BICR IN THE OVERALL POPULATION (COHORTS A+B)



No. at risk											
Olaparib	256	188	145	106	67	48	31	21	11	2	0
Physician's choice	131	73	38	20	9	5	5	3	2	1	0

	Olaparib (N=256)	Physician's choice (N=131)
Events (%)	180 (70.3)	99 (75.6)
Median PFS (months)	5.82	3.52
Hazard ratio (95% CI)	0.49 (0.38, 0.63) *P*<0.0001	

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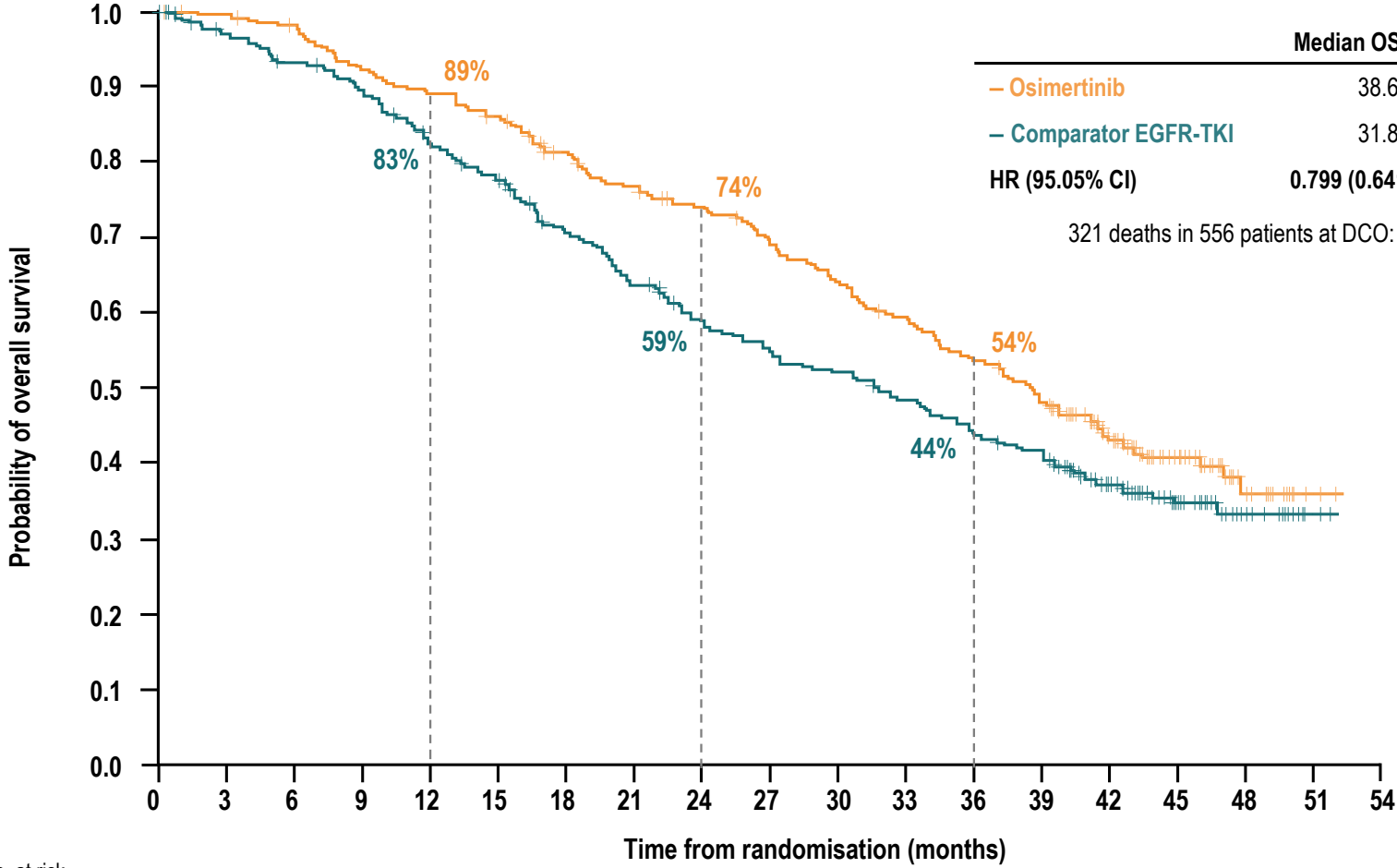
Tagrisso's Phase III FLAURA trial

OVERALL SURVIVAL



	Median OS, months (95% CI)
– Osimertinib	38.6 (34.5, 41.8)
– Comparator EGFR-TKI	31.8 (26.6, 36.0)
HR (95.05% CI)	**0.799 (0.641, 0.997); p=0.0462**

321 deaths in 556 patients at DCO: 58% maturity

No. at risk																		
Osimertinib	279	276	270	254	245	236	217	204	193	180	166	153	138	123	86	50	17	2	0
Comparator EGFR-TKI	277	263	252	239	219	205	182	165	148	138	131	121	110	101	72	40	17	2	0

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FLAURA data cut-off: 25 June 2019
For statistical significance, a p-value of less than 0.0495, determined by O'Brien-Fleming approach, was required

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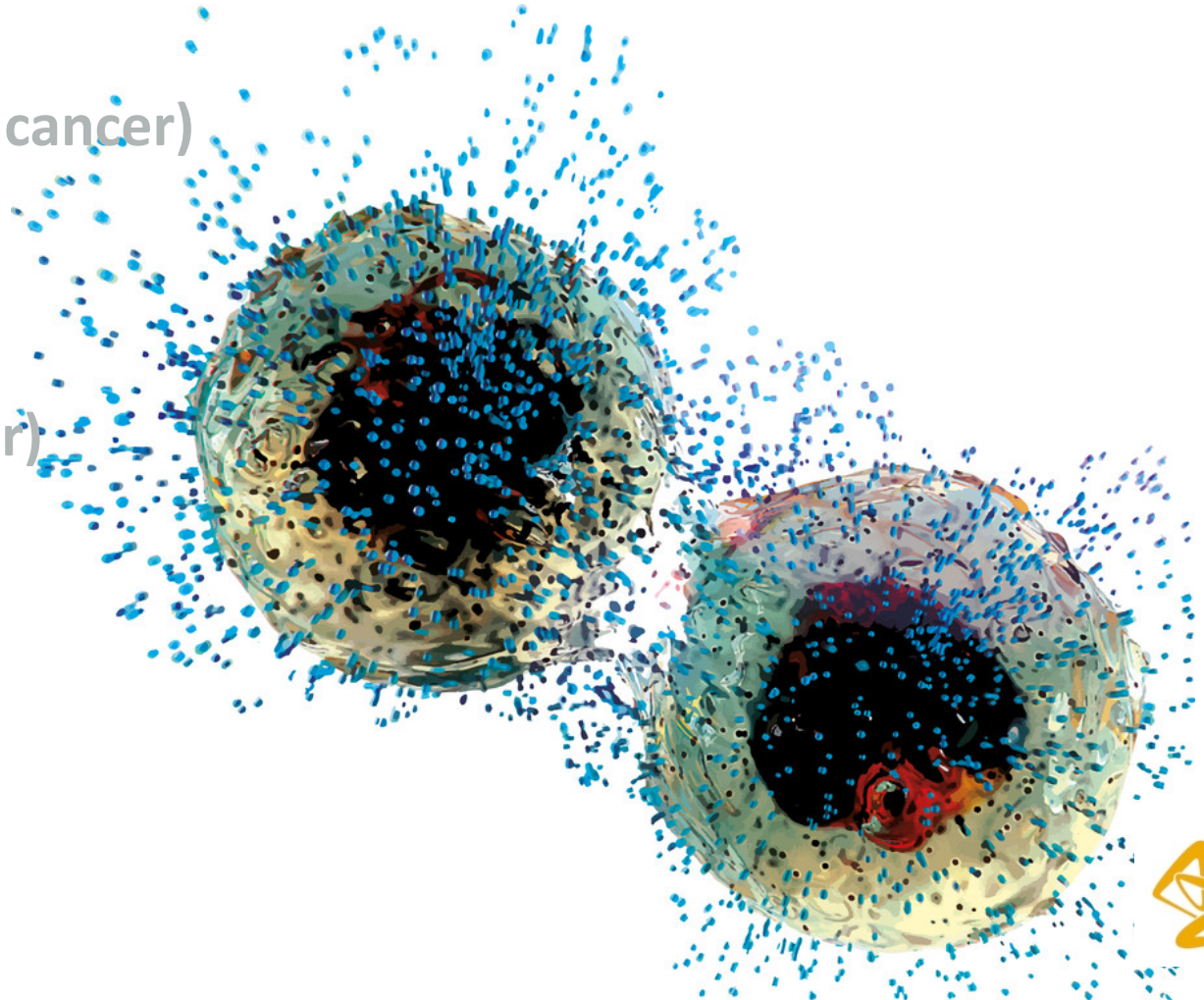
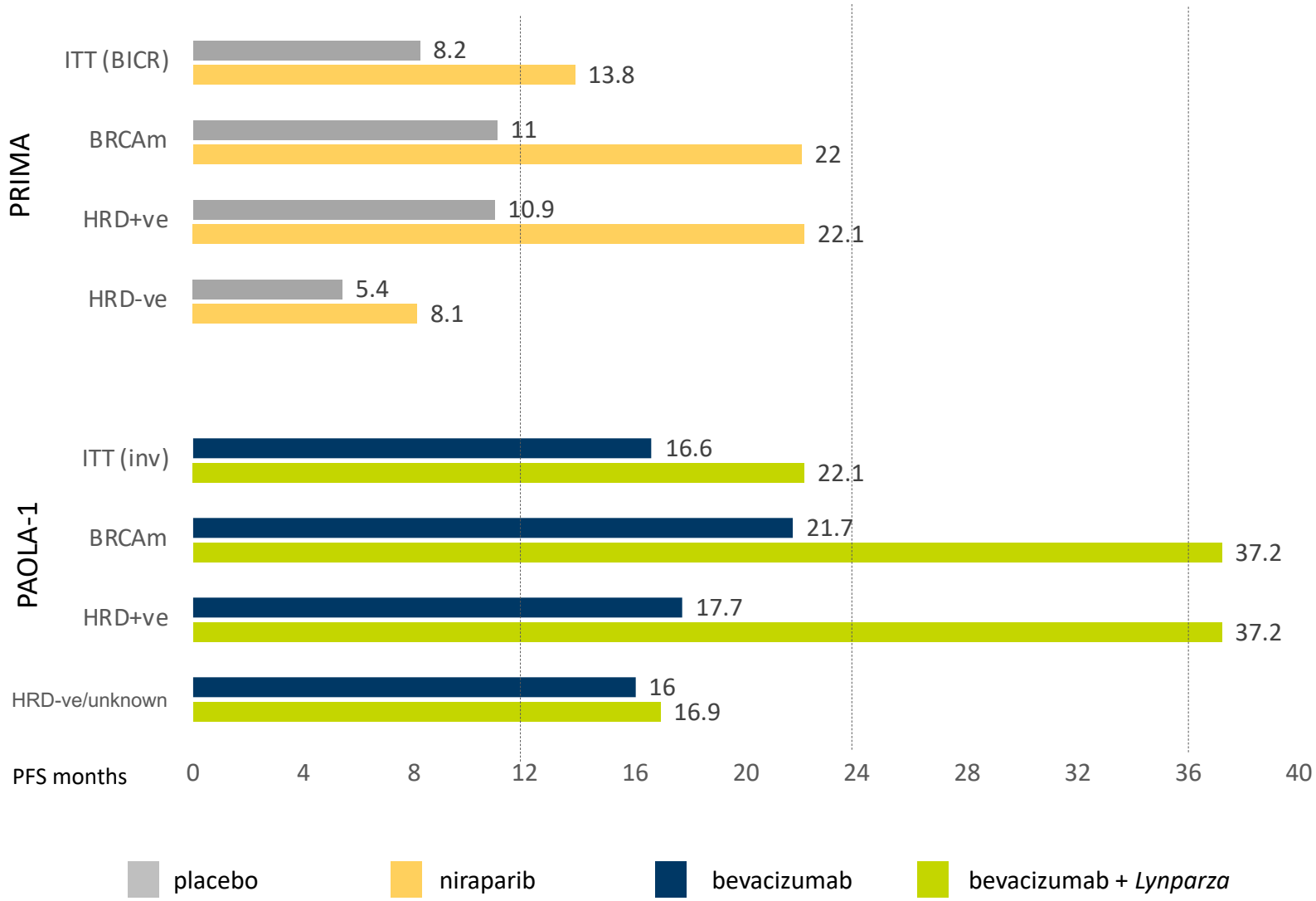


Summary | 1

Median PFS (mPFS) from PRIMA and PAOLA-1 trials



	Difference in mPFS	PFS Hazard Ratio
ITT (BICR)	5.6m (BICR)	0.62 (BICR)
BRCAm	11.0m	0.40
HRD+ve	11.2m	0.43
HRD-ve	2.7m	0.68
ITT (inv)	5.5m (BICR: 7.8m)	0.59 (BICR: 0.63)
BRCAm	15.5m	0.31
HRD+ve	19.5m	0.33
HRD-ve/unknown	0.9m	0.92*

Inv: investigator assessed. * Unadjusted.
Source: ESMO 2019.

Summary | 2

Lynparza safety supports general combinability with other medicines

	PRIMA		PAOLA-1	
	niraparib	placebo	bevacizumab + *Lynparza*	bevacizumab
Duration of follow up	13.8months*		24.0m	22.7m
Discontinuation rates for reasons other than disease progression*	18%*	5%*	24%	9%
Due to AE	12%	2%	20%	5%
Withdrew / Other Reasons	6%	3%	4%	4%
Dose reductions	71%	8%	41%	7%
Dose interruptions	80%	18%	54%	24%
AE rates				
≥ Grade 3 (with >10% pts in either trial)	71%	19%	57%	51%
Anaemia	31%	2%	17%	<1%
Neutropenia	13%	1%	6%	3%
Thrombocytopenia	29%	<1%	2%	<1%
Platelet count decrease	13%	<1%	Grouped as thrombocytopenia	Grouped as thrombocytopenia
Hypertension	NR	NR	19%	30%

Source: ESMO 2019, González-Martín et al. NEJM; 28 September 2019.

Summary | 3

New options for 1st-line ovarian cancer maximising chance of cure or long-term remission

	Bevacizumab eligible ~70 to 80%	Bevacizumab ineligible ~20 to 30%
BRCAm/HRD+ve and HRD unknown (~65%)	*Lynparza* + bevacizumab	*Lynparza* / niraparib monotherapy
Known HRD-ve (~35%)	bevacizumab monotherapy	niraparib monotherapy

Illustrative; AstraZeneca estimates.

Summary | 4

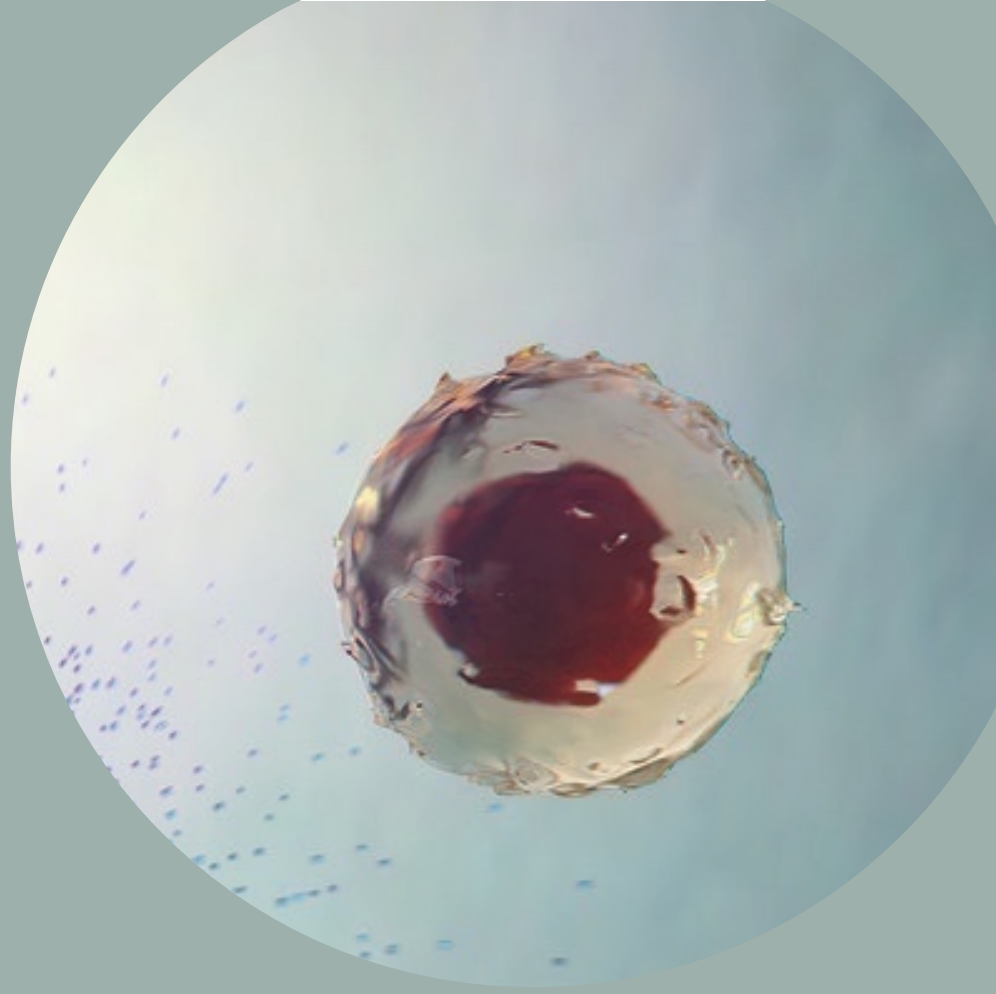
Phase III data presented at ESMO 2019

- *Lynparza* Phase III PAOLA-1 trial (ovarian cancer)
  - Bevacizumab + *Lynparza* demonstrated unprecedented median PFS in 1st-line maintenance OC[1] of >22 months in a representative ovarian cancer population not restricted by surgical outcome, with additional benefit in HRD positive patients
  - *Lynparza* is the only PARPi[2] with Phase III OC data as monotherapy in BRCAm or when combined with bevacizumab in all-comers patients
  - *Lynparza* is generally well tolerated with or without bevacizumab; safety was consistent with previous trials and the addition of *Lynparza* to bevacizumab did not impact on bevacizumab tolerability and health-related quality of life
- *Lynparza* Phase III PROfound trial (prostate cancer)
  - First time a positive Phase III in biomarker-selected mCRPC, in patients with BRCA1, BRCA2 and/or ATM alterations
- *Tagrisso* Phase III FLAURA trial (lung cancer)
  - Unprecedented ORR, PFS and now OS reinforces *Tagrisso* as the standard of care in 1st-line EGFRm NSCLC patients

Continuing to improve standards of care for oncology patients

1. Ovarian cancer. 2. Poly (ADP-ribose) polymerase inhibitor.

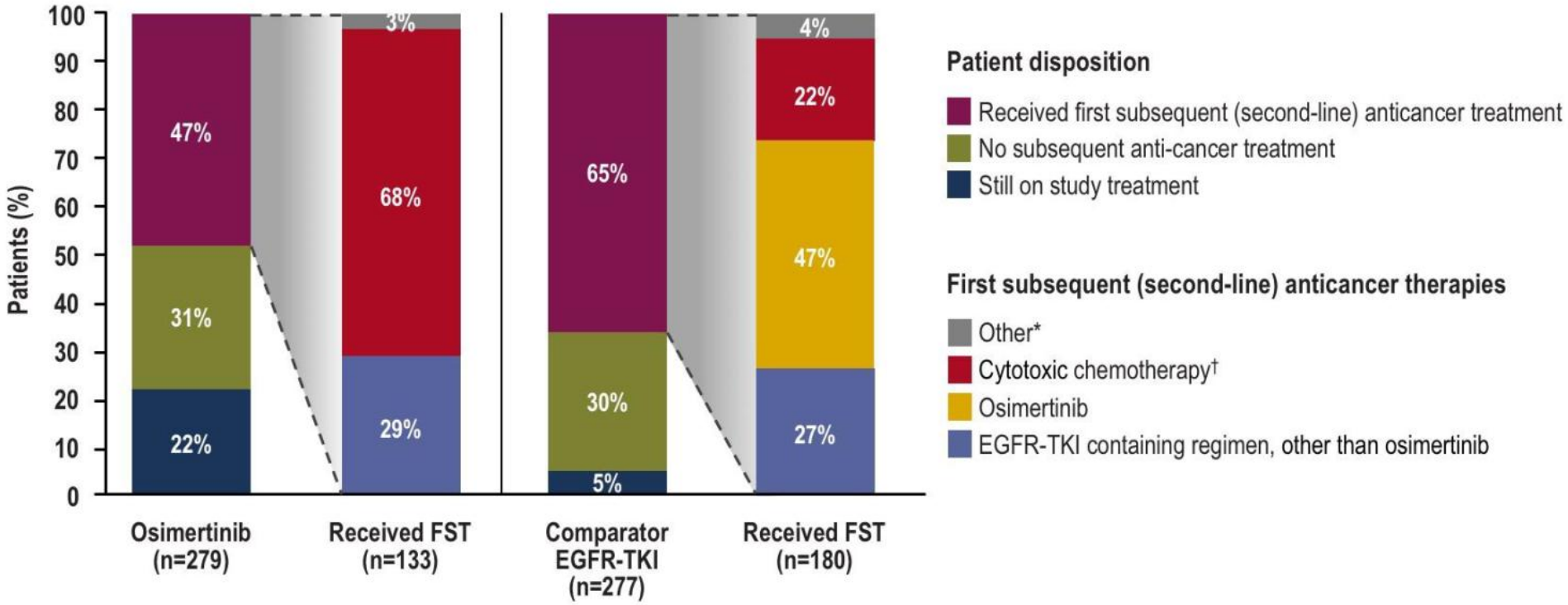
Q&A



Appendix: *Tagrisso*'s Phase III FLAURA trial

SECOND-LINE TREATMENT FOLLOWING PROGRESSION

- Of the 180 patients in the comparator EGFR-TKI arm who received a first subsequent treatment, **85 patients (47%) crossed over to osimertinib** (31% of all patients randomised from the comparator EGFR-TKI arm)



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*Refers to those patients who did not receive either chemotherapy or an EGFR-TKI; †The majority of patients who received cytotoxic chemotherapy received a platinum-based chemotherapy regimen
FST, first subsequent treatment

Data cut-off: 25 June 2019

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Use of AstraZeneca conference call, webcast and presentation slides