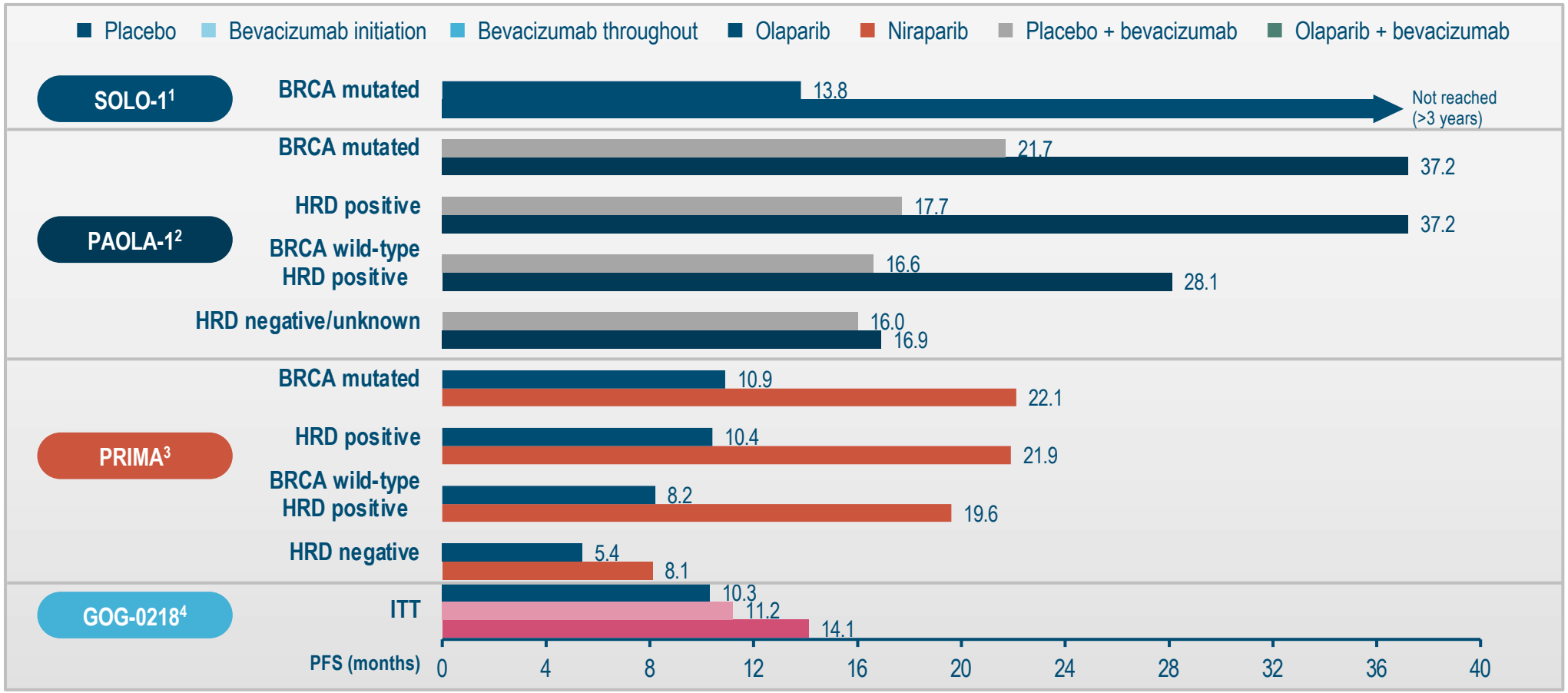
SLIDES FOR OVARIAN (RTP) – ROBERT L. COLEMAN MD

- PRIMA update
- PAOLA-1 update
- VELIA
- OVARIO
- SOLO-1 update
- Mirvetuximab/Bevacizumab update
- MEDIOLA update
- KEYNOTE-100
- Nivo vs Nivo/Ipi

SUMMARY OF APPROVED MAINTENANCE STUDIES IN THE FIRST-LINE



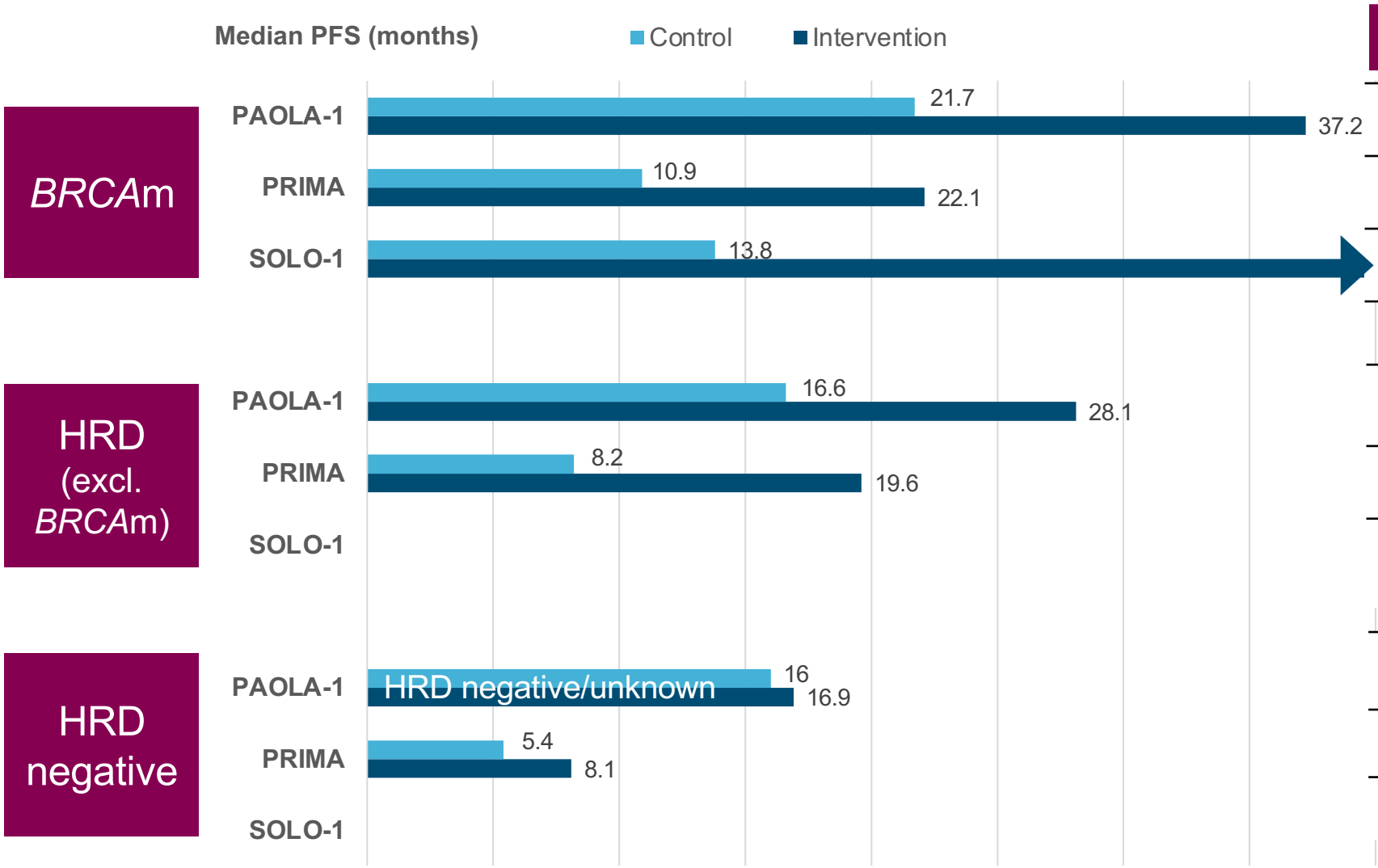
Comparisons across trials should not be made as trials were not head-to-head.

BRCA, breast cancer gene; HRD, homologous recombination deficiency; ITT, intent-to-treat; PFS, progression-free survival

1. Moore K, et al. N Engl J Med 2018;379:2495–2505; 2. Ray-Coquard IL, et al. N Engl J Med 2019; 381:2416–2428; 3. Gonzalez-Martin A, et al. N Engl J Med 2019;381:2391–2402; 4. Burger RA, et al. N Engl J Med 2011;365:2473–2483

Courtesy of Robert L Coleman, MD

PREDICTIVE BIOMARKER: BRCA-MUTATION



Δ mPFS (mo)	HR
15.5	0.31
11.2	0.40
NE	0.30
11.5	0.43
11.4	0.50
0.9	0.92
2.7	0.68

BRCA = breast cancer susceptibility gene; BRCAm = BRCA mutation; HRD = homologous recombination deficiency; mPFS = median progression-free survival; PARP = poly ADP-ribose polymerase.

1. Moore K et al. N. Engl. J. Med. 2018;379:2495-2505; 2. Gonzalez-Martin A, et al. N Engl J Med. 2019;381(25):2391-2402; 3. Gonzalez-Martin A, et al. Presented at: ESMO; 27 September–1 October 2019; Barcelona, Spain. Abstract LBA1;
4. Ray-Coquard I, et al. N Engl J Med. 2019;381:2416-28; 5. Ray-Coquard I, et al. Presented at: ESMO; 27 September–1 October 2019; Barcelona, Spain. Abstract LBA2

Courtesy of Robert L Coleman, MD

SOLO-1: STUDY DESIGN

- Newly diagnosed, FIGO stage III–IV, high-grade serous or endometrioid ovarian, primary peritoneal or fallopian tube cancer*
- **Germline or somatic *BRCA*m**
- ECOG performance status 0–1
- In clinical complete response or partial response after platinum-based chemotherapy

Maintenance therapy

Randomize 2:1

Stratification:
- Response to platinum-based chemotherapy

Olaparib 300 mg bid (N=260)

Placebo (N=131)

- Study treatment continued until disease progression
- Patients with no evidence of disease at 2 years stopped treatment
- Patients with a partial response at 2 years could continue treatment

Primary endpoint

- Investigator-assessed PFS (modified RECIST 1.1)

Secondary endpoints

- PFS using BICR
- PFS2
- Overall survival
- Time from randomization to first subsequent therapy or death
- Time from randomisation to second subsequent therapy or death
- HRQoL (FACT-O TOI score)

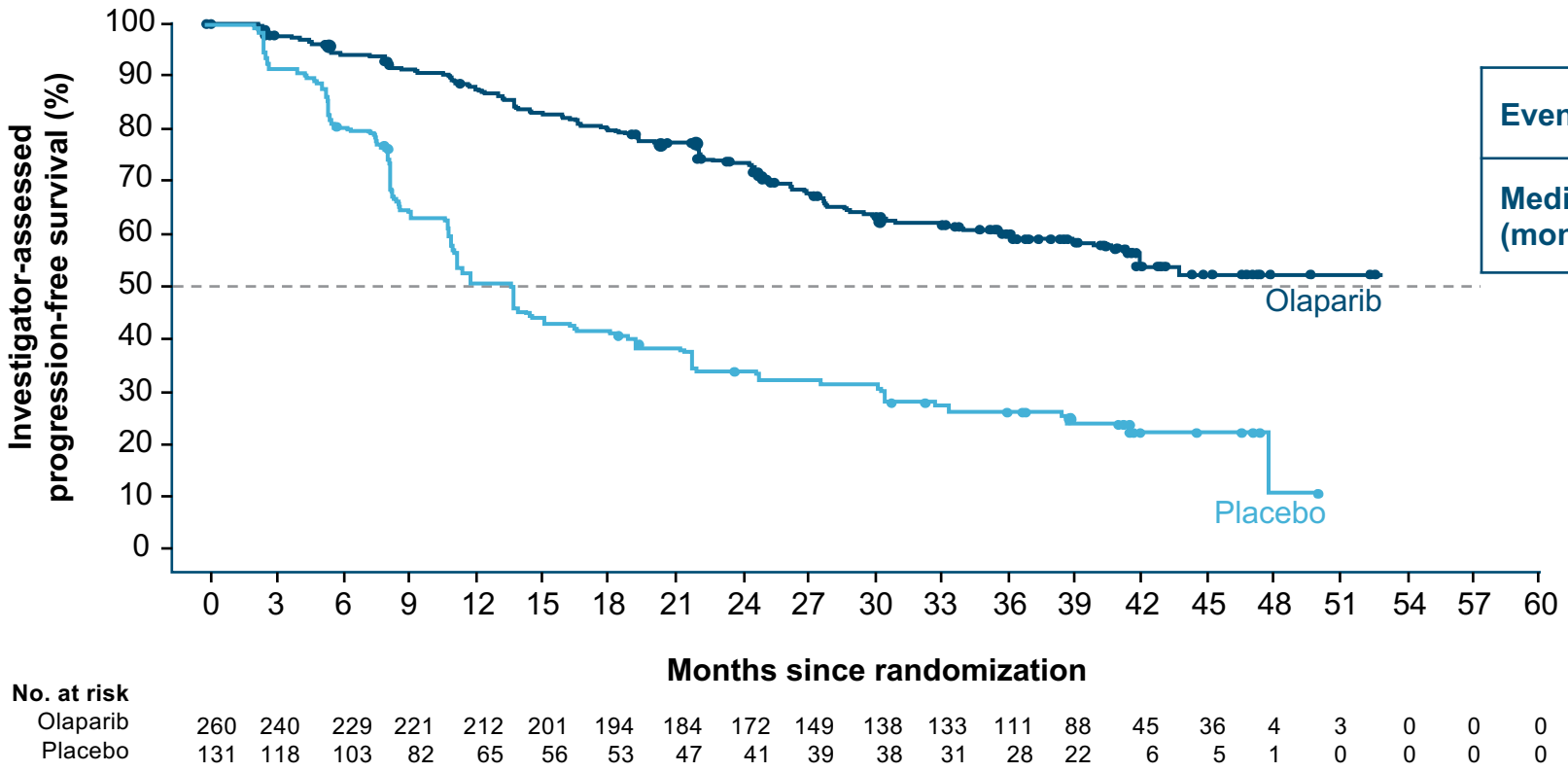
*Upfront or interval attempt at optimal cytoreductive surgery for stage III disease and either biopsy and/or upfront or interval cytoreductive surgery for stage IV disease.
BICR = blinded independent central review; BRCA = breast cancer susceptibility gene; BRCAm = BRCA mutation; ECOG = Eastern Cooperative Oncology Group; FACT-O = Functional Assessment of Cancer Therapy – Ovarian Cancer; FIGO = International Federation of Gynecology and Obstetrics; HRQoL = health-related quality of life; ; PARP = poly (ADP-ribose) polymerase; PFS = progression-free survival; PFS2 = time to second progression or death; RECIST = Response Evaluation Criteria in Solid Tumours; TOI = Trial Outcome Index.

1. NCT0184486. clinicaltrials.gov. Accessed November 2018; 2. Moore K et al. N. Engl. J. Med. 2018;379:2495-2505.

Courtesy of Robert L Coleman, MD

SOLO-1: PFS BY INVESTIGATOR ASSESSMENT

OLAPARIB REDUCED HAZARD OF PROGRESSION OR DEATH BY 70% VS PLACEBO



	Olaparib	Placebo
Events, N (%)	102 (39.2)	96 (73.3)
Median PFS (months)	NR	13.8
	HR=0.30 95% CI: 0.23, 0.41 P<0.001	

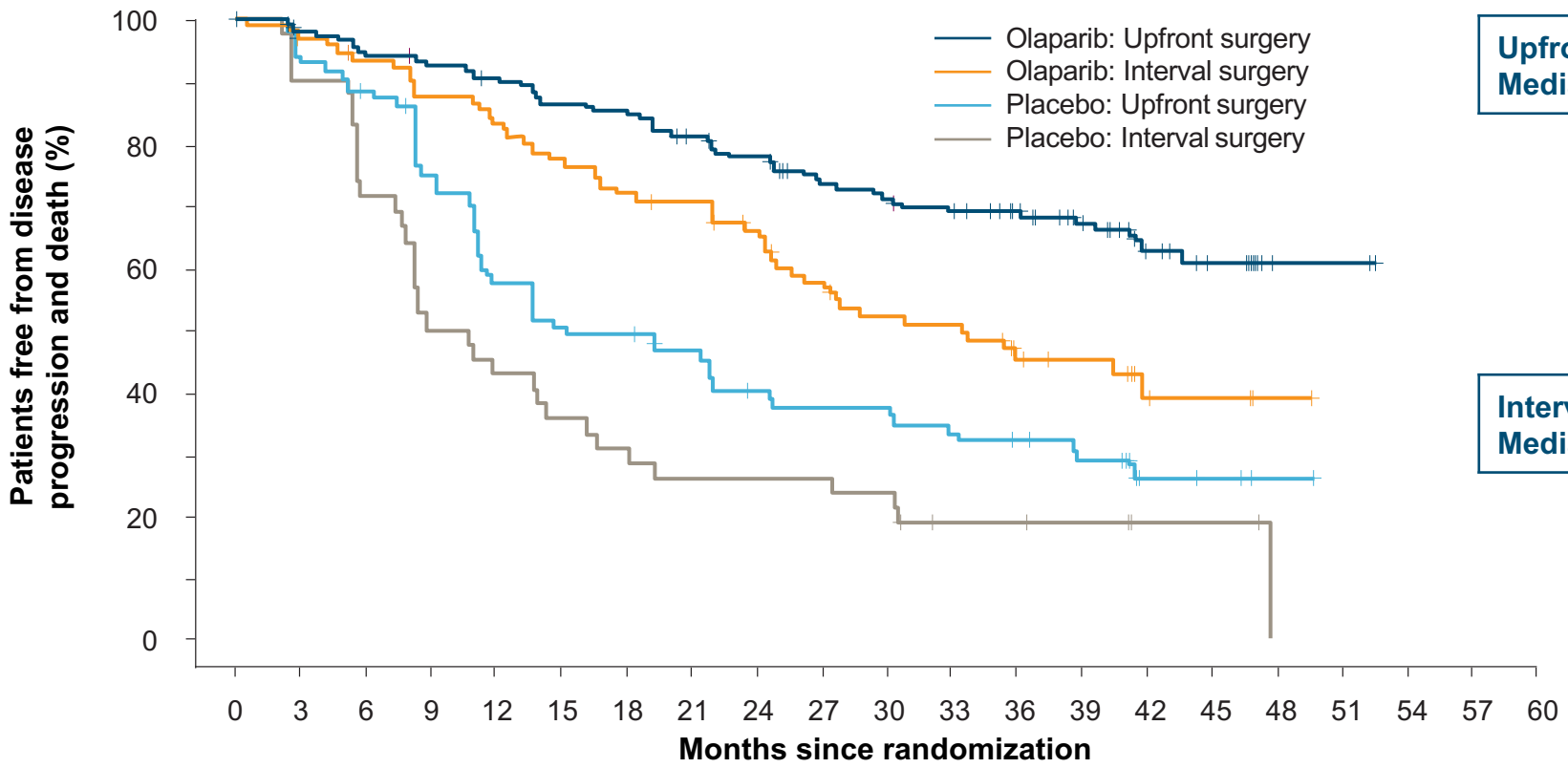
Primary endpoint:
investigator-assessed PFS

Analysis of ITT population (ie, BRCAm). DCO: May 2018; Median FU: olaparib, 40.7 months placebo, 41.2 months
Analysis was performed after 198 progression events had occurred (in 50.6% of patients)
CI = confidence interval; DCO = data cut-off; HR = hazard ratio; ITT = intention to treat; NR = not reached; PFS = progression-free survival

1. Moore K et al. N. Engl. J. Med. 2018;379:2495-2505; 2. Moore K et al. Oral presentation LBA7_PR, ESMO (2018).

Courtesy of Robert L Coleman, MD

SOLO-1: REGARDLESS OF SURGERY TIMING, OLAPARIB IMPROVED PROGRESSION-FREE SURVIVAL VS PLACEBO



No. at risk:																				
Olaparib: Upfront surgery	161	148	142	139	135	129	127	119	113	100	96	92	79	66	34	26	3	3	0	0	0
Olaparib: Interval surgery	94	87	82	77	73	68	63	61	55	45	40	39	30	21	10	0	1	0	0	0	0
Placebo: Upfront surgery	85	78	73	61	47	41	40	36	30	28	28	25	22	17	4	3	1	0	0	0	0
Placebo: Interval surgery	43	38	30	21	18	15	13	11	11	11	10	6	6	5	2	2	0	0	0	0	0

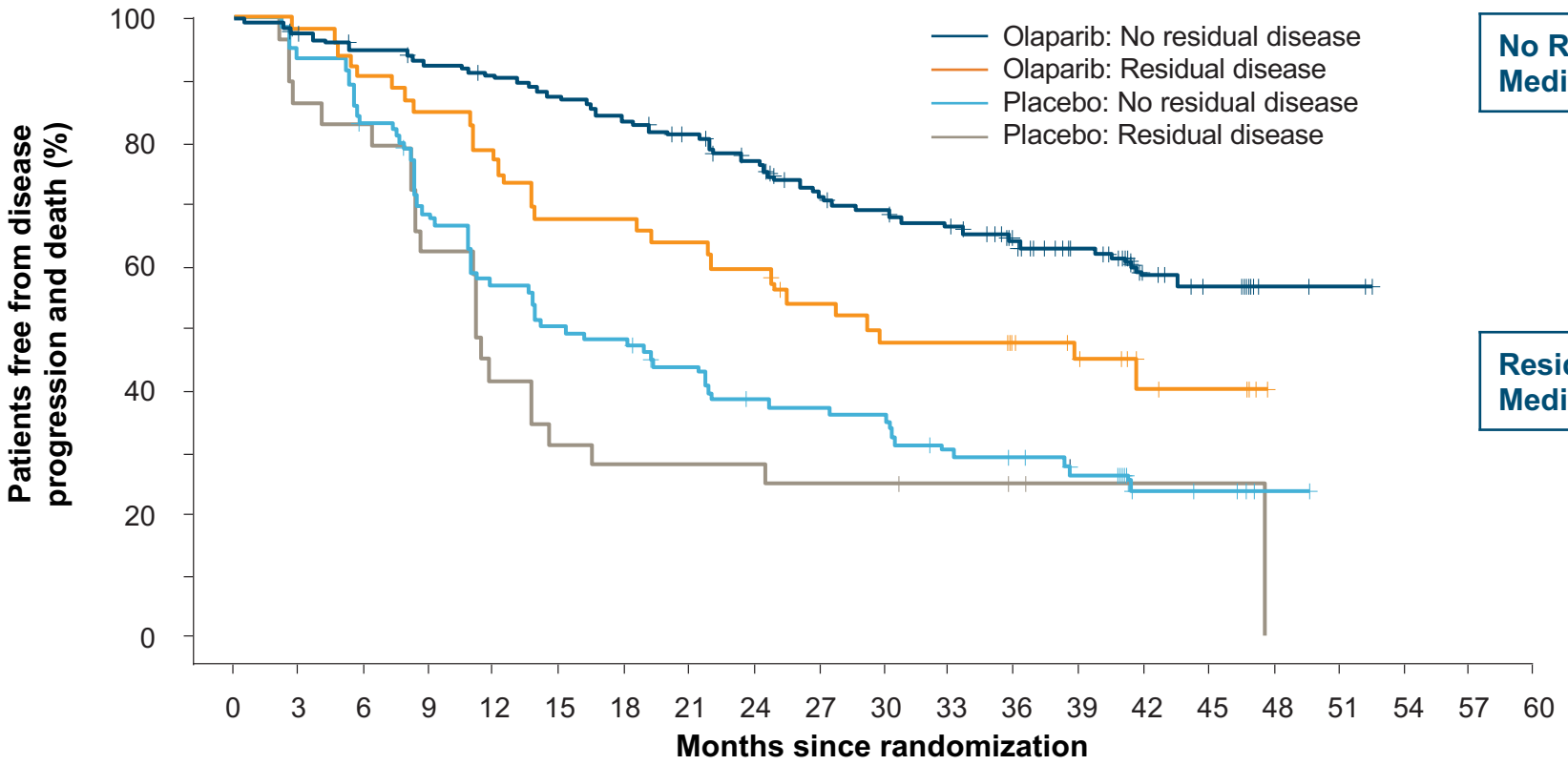
	Olaparib	Placebo
Upfront Surgery: Median PFS (mo)	NR	15.3
	HR = 0.31 95% CI: 0.21–0.46	

	Olaparib	Placebo
Interval Surgery: Median PFS (mo)	33.6	9.8
	HR = 0.37 95% CI: 0.24–0.58	

Investigator-assessed PFS.
CI = confidence interval; HR = hazard ratio; NR = not reached; PFS = progression-free survival.
1. Mathews C, et al. 2019 ASCO Annual Meeting. Poster 5541

Courtesy of Robert L Coleman, MD

SOLO-1: OLAPARIB IMPROVED PROGRESSION-FREE SURVIVAL VS PLACEBO REGARDLESS OF SURGICAL OUTCOME



No. at risk:																				
Olaparib: No residual disease	200	184	177	172	167	162	155	147	137	119	113	108	90	70	36	28	4	3	0	0	0
Olaparib: Residual disease	55	51	47	44	41	35	35	33	31	26	23	23	19	16	8	7	0	0	0	0	0
Placebo: No residual disease	98	90	79	64	53	47	45	39	33	32	31	25	23	18	5	4	1	0	0	0	0
Placebo: Residual disease	29	25	24	18	12	9	8	8	8	7	7	6	5	4	1	1	0	0	0	0	0

	Olaparib	Placebo
No Residual Disease: Median PFS (mo)	NR	15.3
	HR = 0.33 95% CI: 0.23–0.46	

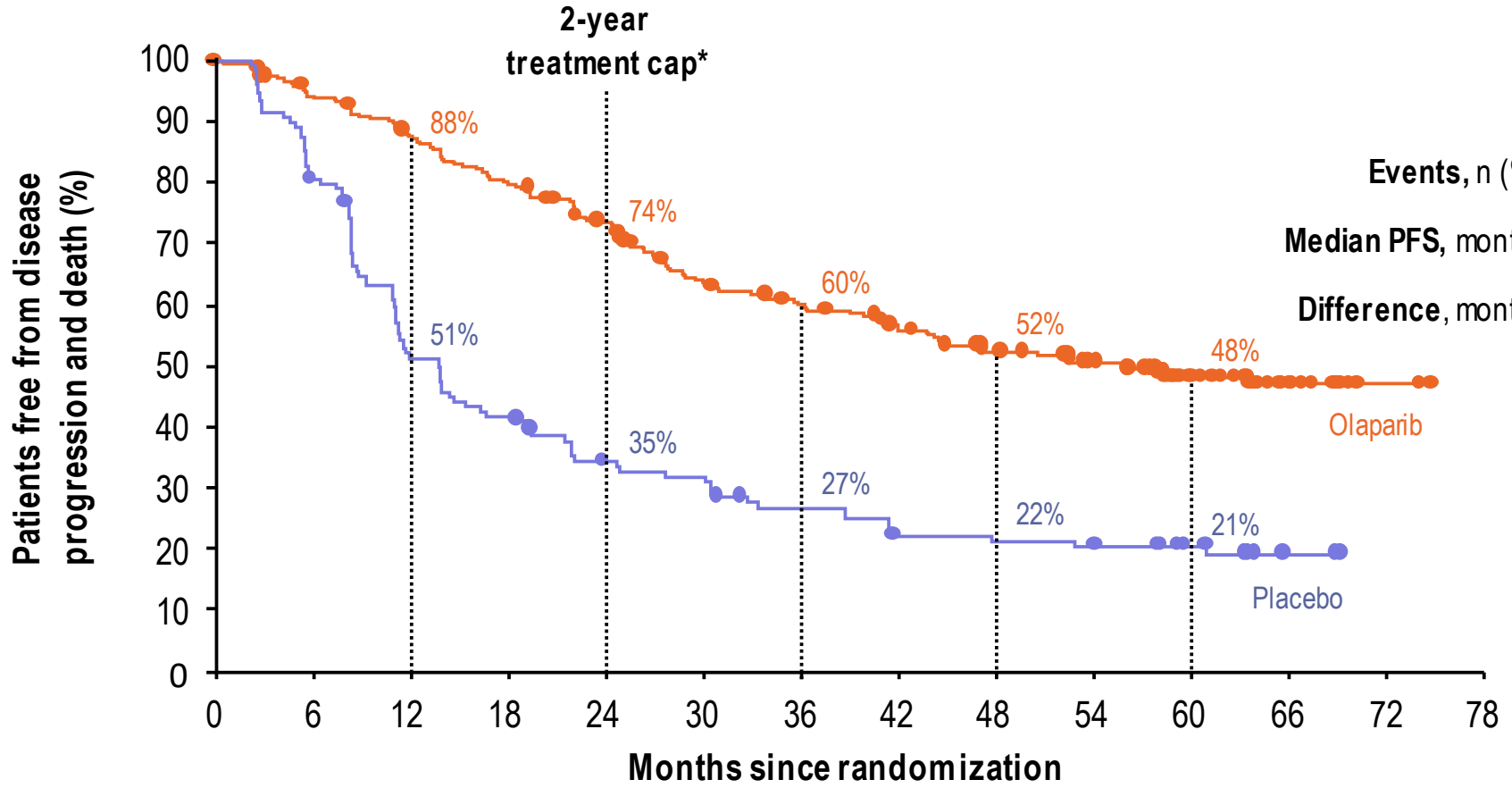
	Olaparib	Placebo
Residual Disease: Median PFS (mo)	29.4	11.3
	HR = 0.44 95% CI: 0.25–0.77	

Investigator-assessed PFS. Surgical outcome was reported by the treating physician.
CI = confidence interval; HR = hazard ratio; NR = not reached; PFS = progression-free survival.

1. Mathews C, et al. 2019 ASCO Annual Meeting. Poster 5541.

Courtesy of Robert L Coleman, MD

SOLO-1: PFS benefit of maintenance Olaparib was sustained beyond the end of treatment



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	118 (45)	100 (76)
Median PFS, months	**56.0**	**13.8**
Difference, months	42.2	
	HR 0.33 (95% CI 0.25–0.43)	

Median treatment duration:
Olaparib, 24.6 months
Placebo†, 13.9 months

No. at risk

Olaparib	260	229	212	194	173	140	129	115	101	91	58	30	2	0
Placebo	131	103	65	53	41	38	30	24	23	22	16	3	0	

*13 patients, all in the olaparib arm, continued study treatment past 2 years; †n=130 (safety analysis set)
Investigator-assessed by modified RECIST v1.1. DCO: 5 March 2020

Courtesy of Robert L Coleman, MD

VIRTUAL 2020 ESMO congress

SOLO-1

Secondary efficacy outcomes* support the observed PFS benefit

	Overall		Patients in CR at baseline	
PFS2	Olaparib (n=260)	Placebo (n=131)	Olaparib (n=189)	Placebo (n=101)
Events, n (%)	80 (31)	61 (47)	49 (26)	45 (45)
Event free at 5 years, %	64	41	68	44
Median, months	NR	42.1	NR	52.9
	HR 0.46 (95% CI 0.33–0.65)		**HR 0.48** (95% CI 0.32–0.71)	
TSST				
Events, n (%)	95 (37)	77 (59)	64 (34)	56 (55)
Event free at 5 years, %	62	36	65	39
Median, months	NR	40.7	NR	47.7
	HR 0.46 (95% CI 0.34–0.63)		**HR 0.50** (95% CI 0.35–0.72)	

Safety profile remained consistent with the primary DCO

n (%)	Olaparib (n=260)	Placebo (n=130)
Any AE	256 (98)	120 (92)
Grade ≥3 AE	103 (40)	25 (19)
Serious AE	55 (21)	17 (13)
AE leading to dose interruption	136 (52)	22 (17)
AE leading to dose reduction	75 (29)	4 (3)
AE leading to treatment discontinuation	30 (12)	4 (3)
MDS/AML	3 (1)	0 (0)
New primary malignancy	7 (3)	5 (4)

No additional cases of MDS/AML reported; incidence remained <1.5%

Follow-up for MDS/AML continued until death due to any cause

*Measured from randomization. AE, adverse event; AML, acute myeloid leukaemia; CR, complete response; MDS, myelodysplastic syndrome. DCO: 5 March 2020

Banerjee, ESMO 2020

Courtesy of Robert L Coleman, MD

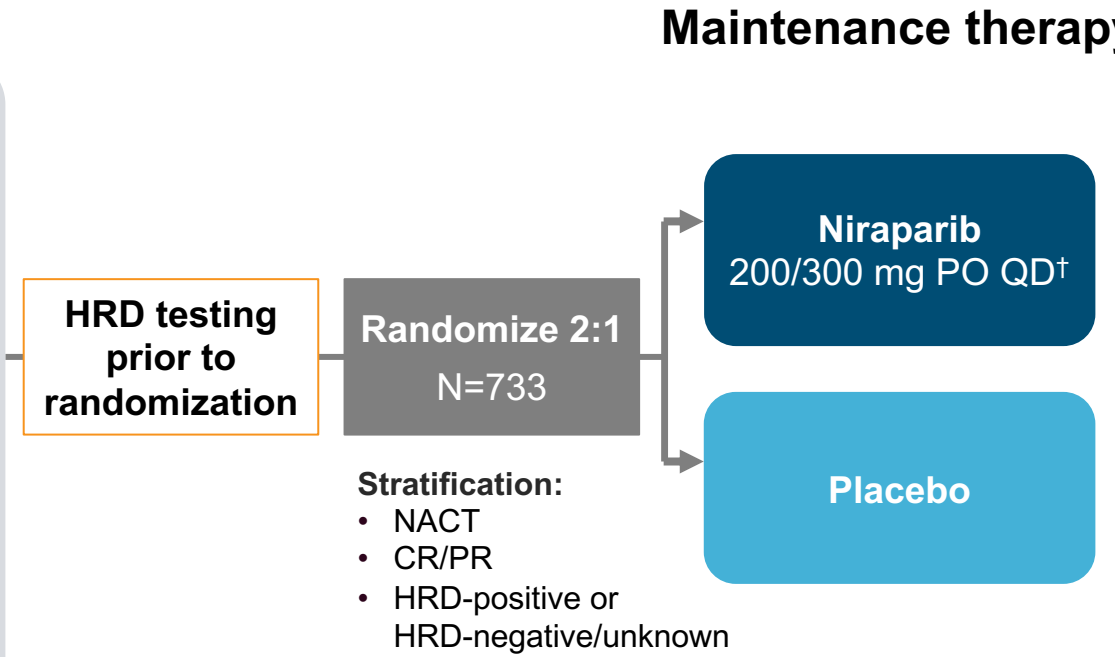
SOLO-1 CONCLUSIONS

- Efficacy from the initial report confirmed with longer follow-up
- Multiple subgroups demonstrate consistent treatment effect
- Safety confirmed
- OS awaited

Courtesy of Robert L Coleman, MD

PRIMA: STUDY DESIGN

- Newly diagnosed, FIGO stage III-IV high-grade serous or endometrioid*
- **Stage III with visible residual disease post-surgery**
- **Inoperable stage III disease**
- Any stage IV disease
- Had received NACT
- CR or PR after platinum-based chemotherapy



Primary endpoint

- PFS (BICR) in **HRD population** and step down to all-comers (RECIST 1.1)

Secondary endpoints

- OS
- PFS2
- TFST
- Safety
- PRO/HRQoL

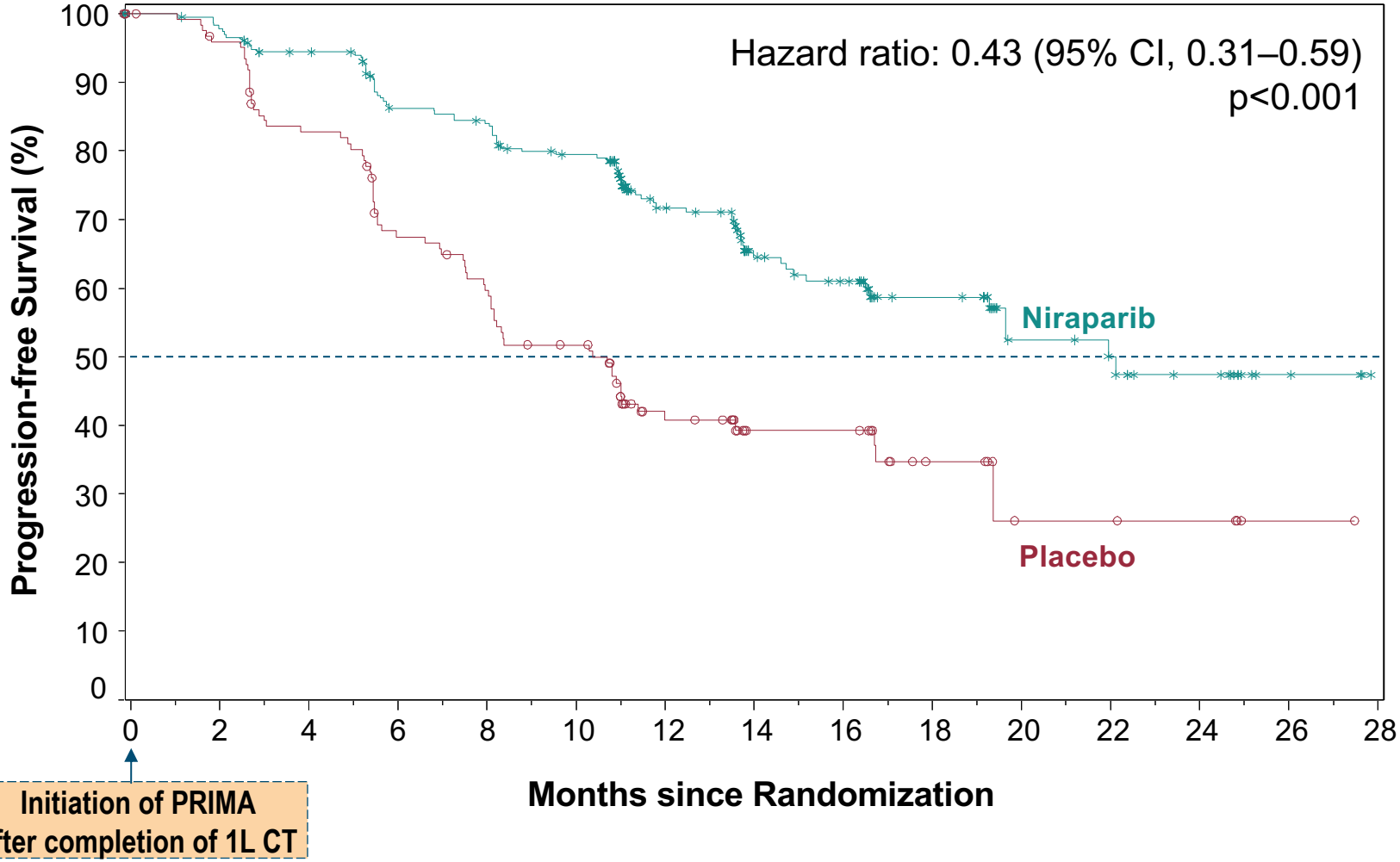
- Patients with stage III disease with no visible residual disease (ie, complete cytoreduction) post-surgery were excluded
- In clinical practice, some physicians would treat PRIMA candidates with chemotherapy + bevacizumab as standard of care

Niraparib is not approved for use outside the platinum-sensitive relapsed ovarian cancer setting.
*Includes patients with primary peritoneal and/or fallopian tube cancer. †Modified starting dose permitted to mitigate for hematological toxicity following protocol amendment.
BICR = blinded independent central review; CA-125 = cancer antigen-125; CR = complete response; FIGO = International Federation of Gynecology and Obstetrics; HRD = homologous recombination deficiency; HRQoL= health-related quality of life; NACT = neoadjuvant chemotherapy; OS = overall survival; PFS = progression-free survival; PFS2 = time to second progression; PR = partial response; PRO = patient-reported outcome; RECIST = Response Evaluation Criteria in Solid Tumours; TFST = time to first subsequent therapy.

1. Gonzalez-Martin A, et al. N Engl J Med. 2019;381(25):2391-2402; 2. Gonzalez-Martin A, et al. Presented at: ESMO; 27 September–1 October 2019; Barcelona, Spain. Abstract LBA1.

Courtesy of Robert L Coleman, MD

PRIMA PRIMARY ENDPOINT: PFS - HRD_{42} POPULATION



57% reduction in hazard of relapse or death with niraparib

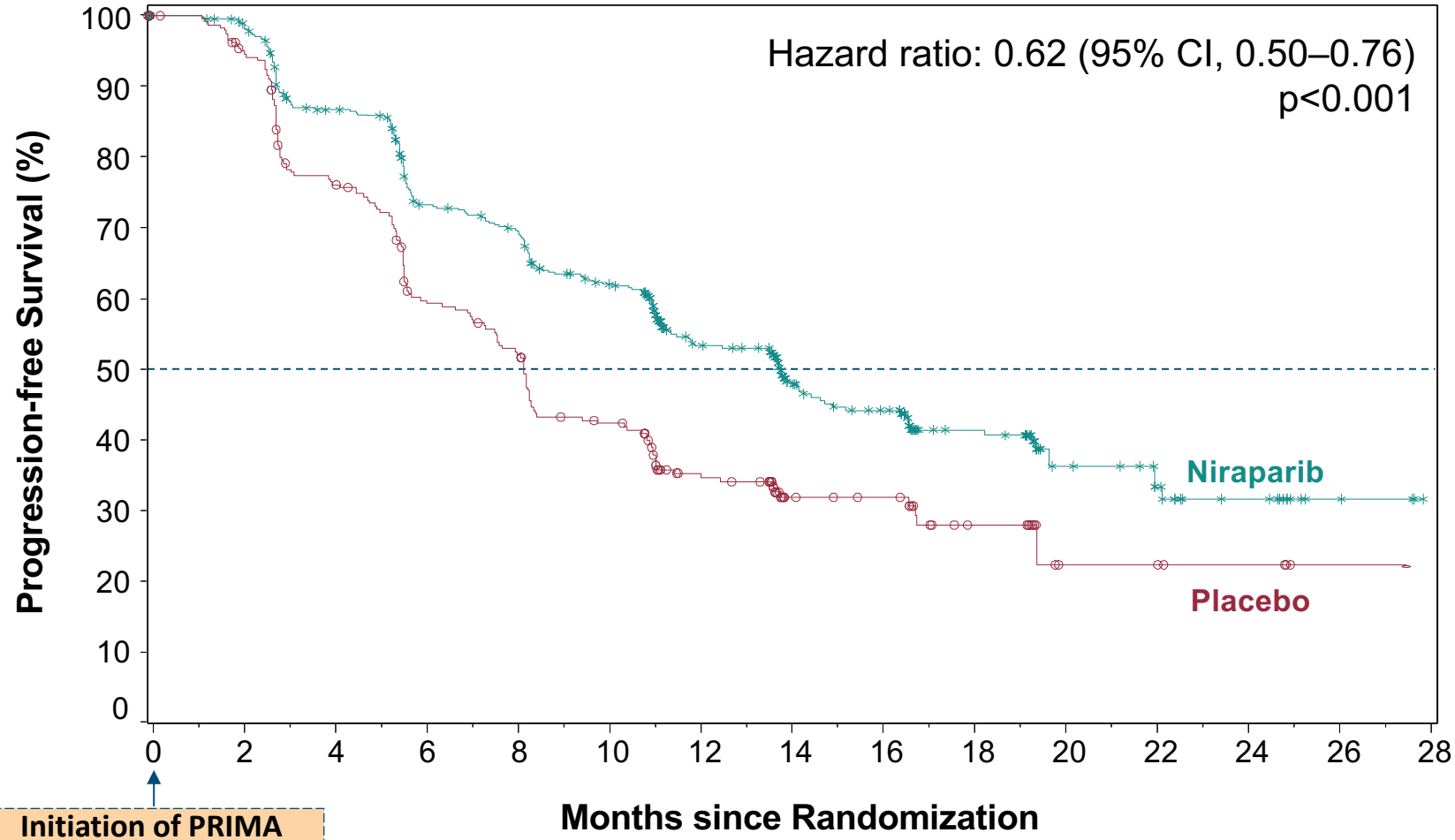
	Niraparib (n=247)	Placebo (n=126)
Median PFS		
months (95% CI)	**21.9 (19.3–NE)**	**10.4 (8.1–12.1)**
Patients without PD or death (%)		
6 months	**86%**	**68%**
12 months	**72%**	**42%**
18 months	**59%**	**35%**

1L, first-line; CI, confidence interval; CT, chemotherapy; HR, homologous recombination; NE, not estimable; PD, progressive disease; PFS, progression-free survival.
Sensitivity analysis of PFS by the investigator was similar to and supported the BICR analysis.

González-Martin, NEJM 2019

Courtesy of Robert L Coleman, MD

PRIMA PRIMARY ENDPOINT: PFS OVERALL POPULATION



Niraparib	487	454	385	312	295	253	167	111	94	58	29	21	13	4	0
Placebo	246	226	177	133	117	90	60	32	29	17	6	6	4	1	0

38% reduction in hazard of relapse or death with niraparib

	Niraparib (n=487)	Placebo (n=246)
Median PFS		
months (95% CI)	**13.8 (11.5–14.9)**	**8.2 (7.3–8.5)**
Patients without PD or death (%)		
6 months	**73%**	**60%**
12 months	**53%**	**35%**
18 months	**42%**	**28%**

1L, first-line; CI, confidence interval; CT, chemotherapy; PD, progressive disease; PFS, progression-free survival.
Discordance in PFS event between investigator assessment vs BICR ≈12%.
González-Martin, NEJM 2019

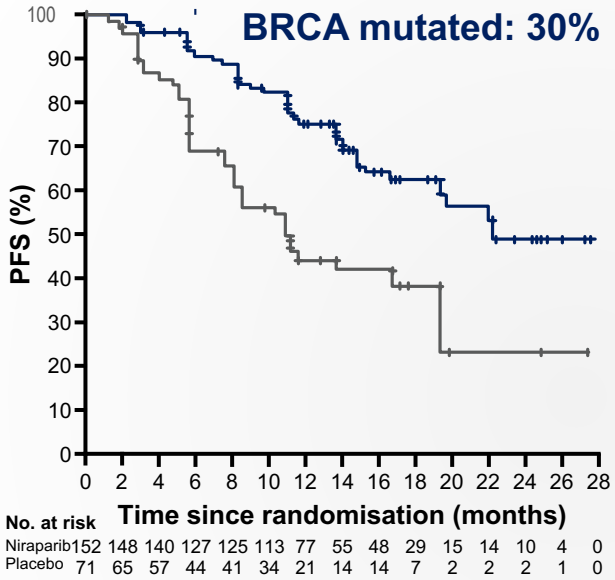
Courtesy of Robert L Coleman, MD

PRIMA: PFS by HRD status (BICR)

Stratification

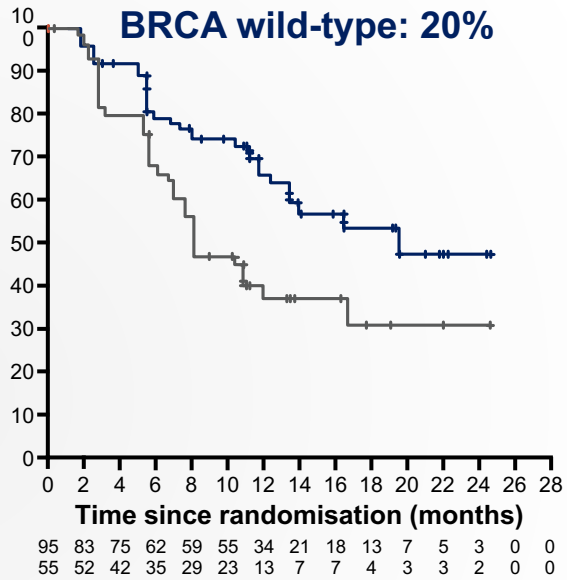
HRD-positive (51%)

BRCA mutated: 30%



	Niraparib (n=152)	Placebo (n=71)
Events, n (%)	49 (32.2)	40 (56.3)
Median PFS, months	**22.1**	**10.9**
Δ Median PFS, months	**11.2 months**	
HR (95% CI)	0.40 (0.27–0.62)	

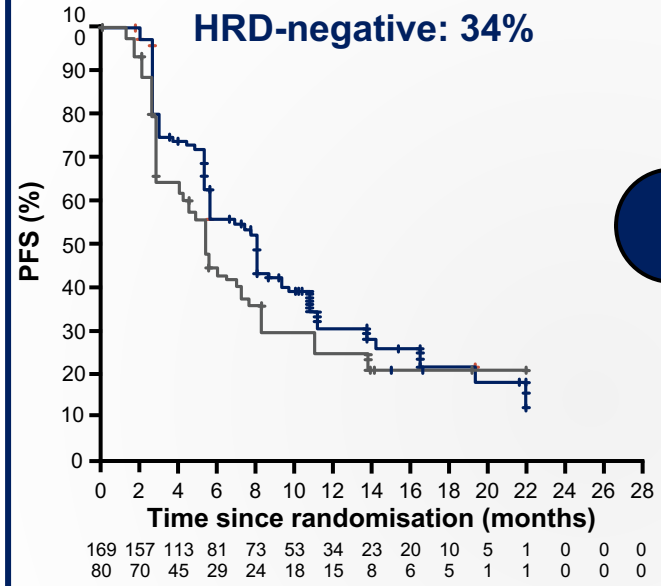
BRCA wild-type: 20%



	Niraparib (n=95)	Placebo (n=55)
Events, n (%)	32 (33.7)	33 (60.0)
Median PFS, months	**19.6**	**8.2**
Δ Median PFS, months	**11.4 months**	
HR (95% CI)	0.50 (0.31–0.83)	

HRD-negative/unknown (49%)

HRD-negative: 34%



	Niraparib (n=169)	Placebo (n=80)
Events, n (%)	111 (65.7)	56 (70.0)
Median PFS, months	**8.1**	**5.4**
Δ Median PFS, months	**2.7 months**	
HR (95% CI)	0.68 (0.49–0.94)	

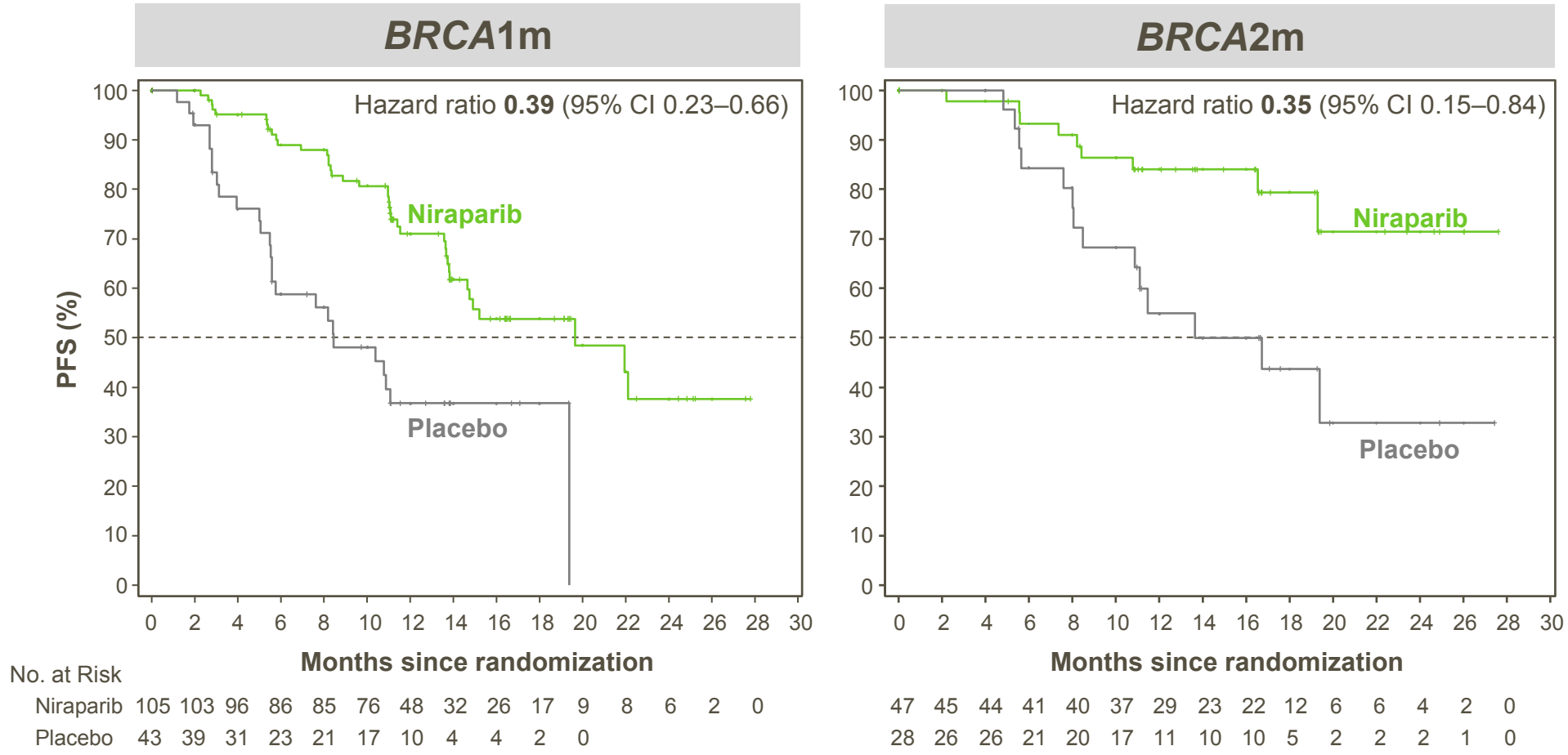
HRD-unknown: 15%

Medians not published
HR 0.85

Courtesy of Robert L Coleman, MD

PRIMA: Efficacy by BRCA mutation status

- **Niraparib efficacy compared to placebo was similar in *BRCA*1m and *BRCA*2m**



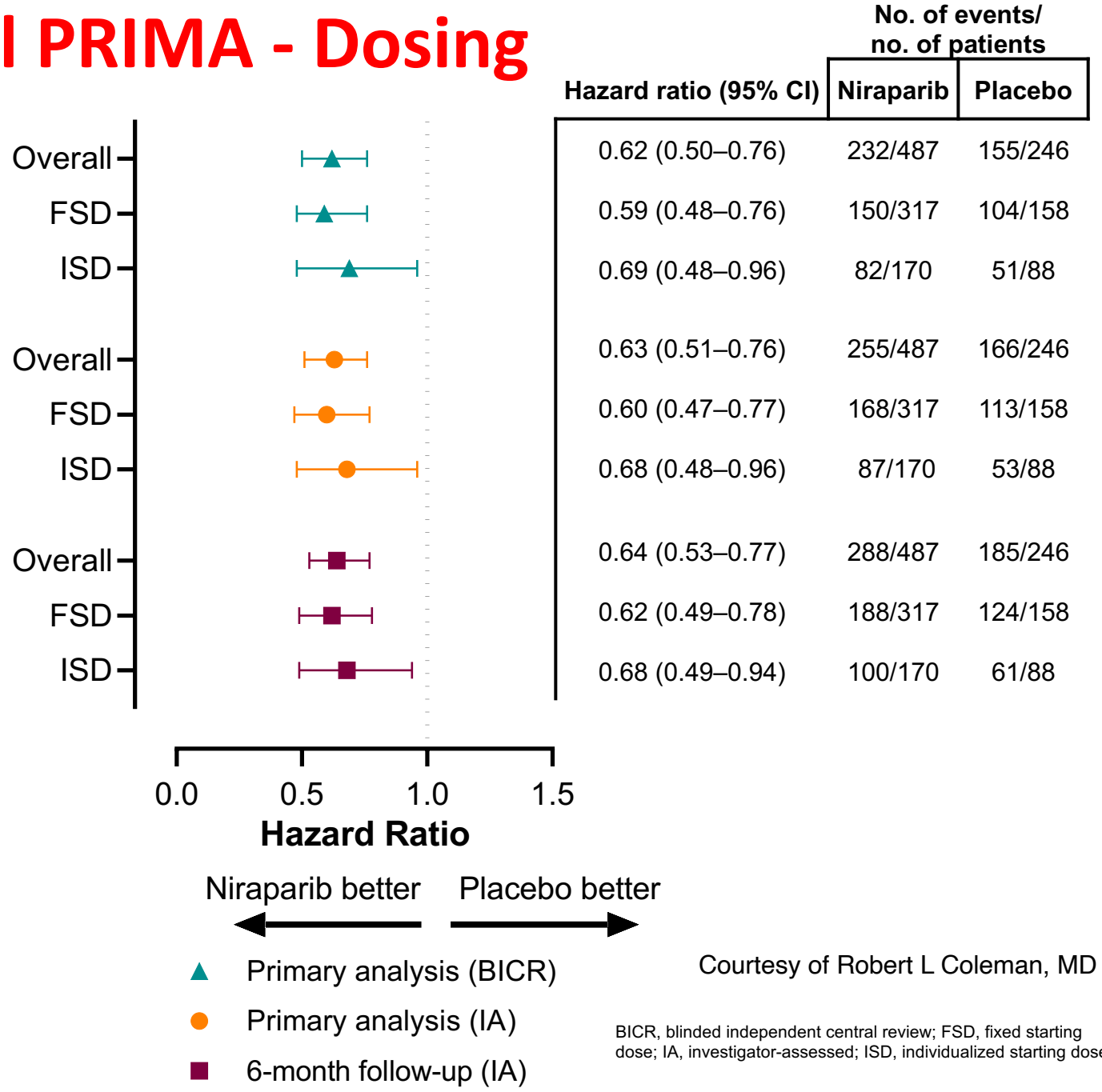
These prespecified subgroup analyses were not powered to detect statistically significant treatment effect; therefore results should be interpreted with caution.

BRCA, breast cancer gene; *BRCA*m, *BRCA* mutant; CI, confidence interval; PFS, progression-free survival.
Monk B, et al. presented at SGO 2020 (Webinar #2), 29 Apr 2020.

Courtesy of Robert L Coleman, MD

Progression-Free Survival PRIMA - Dosing

- No evidence of treatment difference was seen between starting dose regimens
  - A test of treatment interactions between FSD and ISD subgroups did not demonstrate statistical significance at the pre-specified 0.10 level (*P*=0.30)
- BICR and IA PFS were highly concordant
- Primary and updated IA PFS demonstrated sustained efficacy of ISD



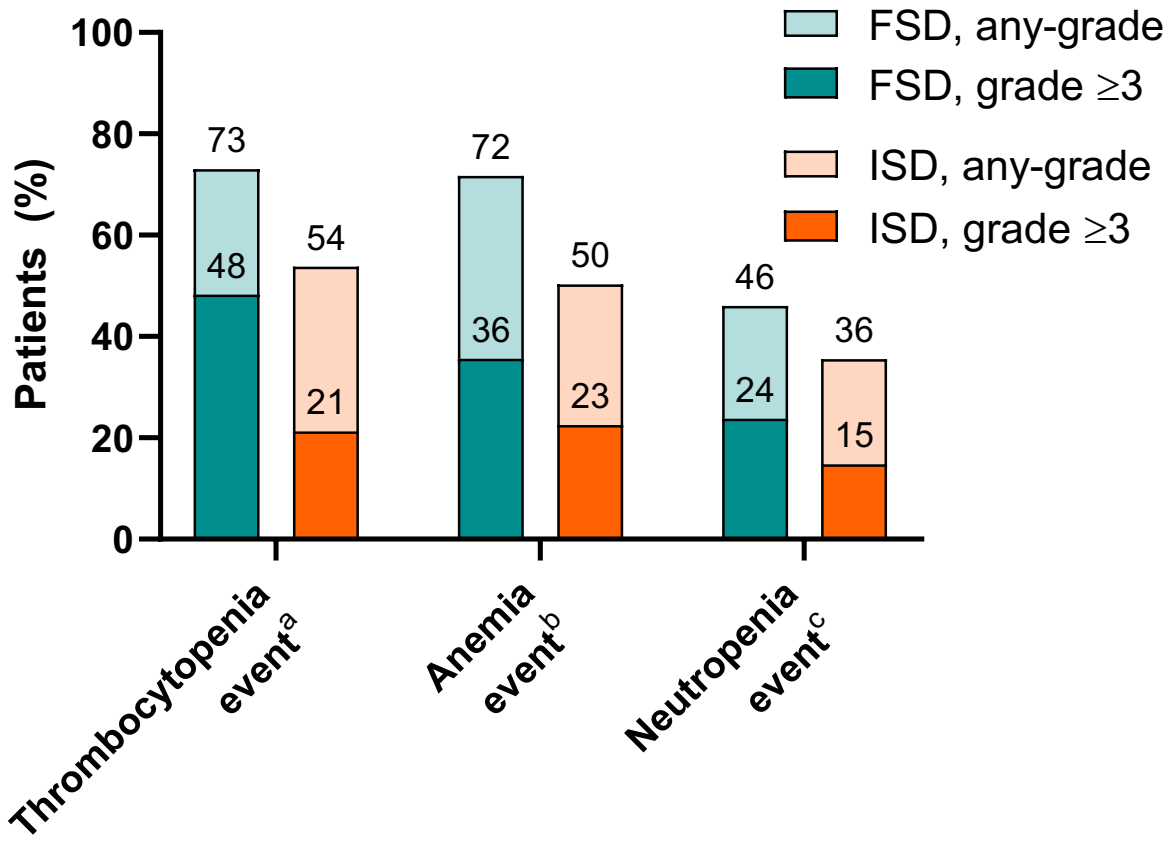
Courtesy of Robert L Coleman, MD

Graybill, IGCS 2020

BICR, blinded independent central review; FSD, fixed starting dose; IA, investigator-assessed; ISD, individualized starting dose.

PRIMA: Safety

- Incidence of any-grade and grade ≥3 hematological TEAEs were reduced with ISD
  - Grade ≥3 thrombocytopenia events reduced from 48.3% to 21.3%
  - Grade ≥3 anemia events reduced from 35.6% to 22.5%
  - Grade ≥3 neutropenia events reduced from 23.8 to 14.8%



Graybill, IGCS 2020

[a]Includes thrombocytopenia and platelet count decreased; [b]Includes anemia and hemoglobin decreased; [c]Includes neutropenia and neutrophil count decreased.
FSD, fixed starting dose; ISD, individualized starting dose.

Courtesy of Robert L Coleman, MD

CONCLUSIONS

- PRIMA Primary endpoints reached in initial trial
- Subgroups show consistent effect particularly in BRCA-mt tumors
  - Strong effect in each *BRCA1* and *BRCA2* (stronger)
- Individualized dosing demonstrates lower toxicity

Courtesy of Robert L Coleman, MD

PAOLA-1: STUDY DESIGN

- Newly diagnosed
- FIGO IIIB-IV high-grade serous/endometrioid ovarian, fallopian tube, or primary peritoneal cancer*
- Surgery (upfront or interval)
- Platinum-taxane based chemotherapy
- **≥3 cycles of bevacizumab**
- NED/CR/PR

Randomize 2:1
N=806

Stratification:
- Tumour *BRCA*m status‡
- First-line treatment outcome¶

Maintenance therapy

Olaparib (300 mg BID) x2 years (N=537)
+ Bevacizumab†

Placebo x2 years (N=269)
+ Bevacizumab†

Primary endpoint

Investigator-assessed PFS (RECIST v1.1)

Sensitivity analysis
PFS by BICR

Secondary endpoints

- TFST
- PFS2, TSST
- OS
- HRQoL
- Safety and tolerability

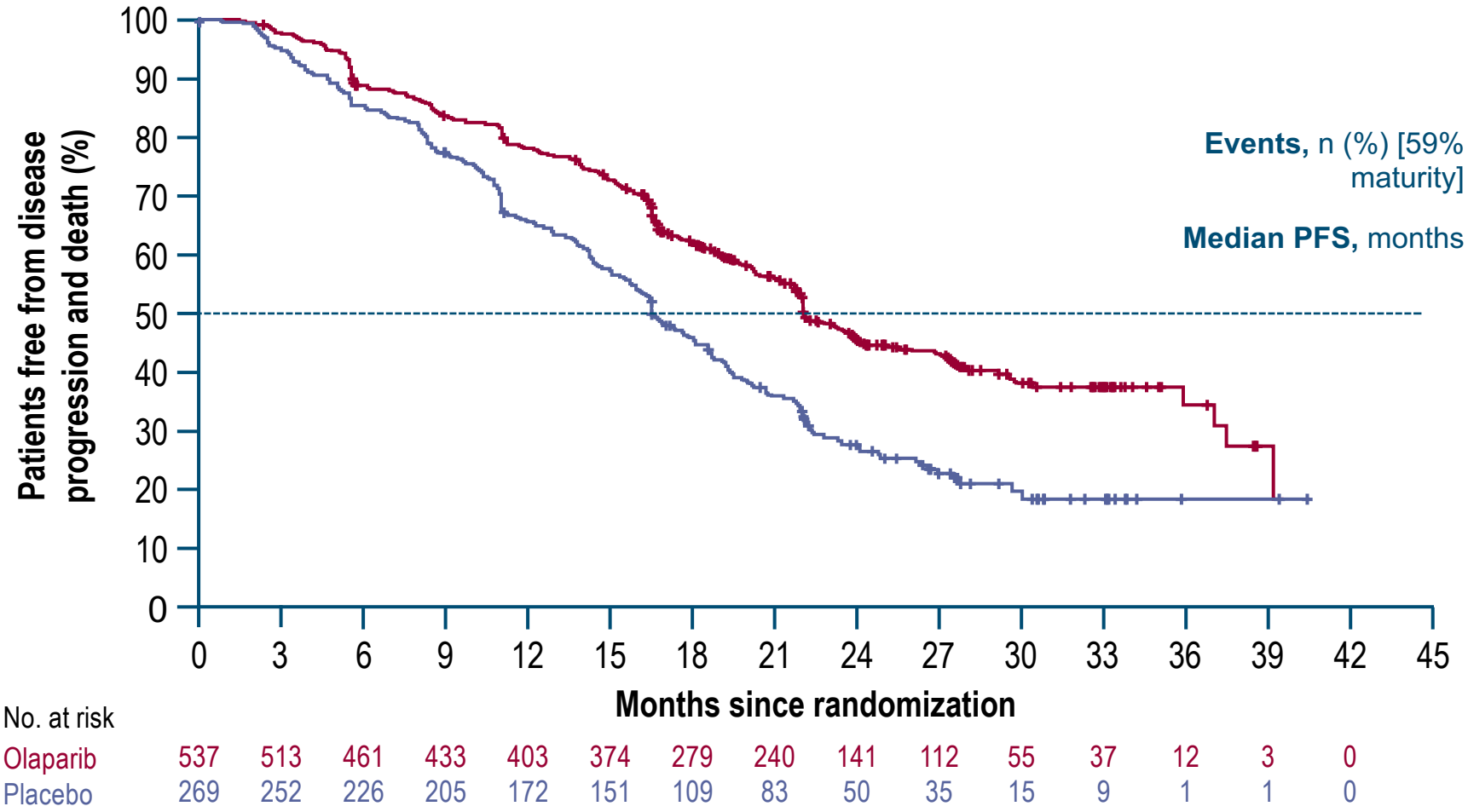
- European-designed study where standard of care includes bevacizumab regardless of patient risk for progression
- PAOLA-1 trial did not evaluate a olaparib monotherapy maintenance arm

Addition of olaparib to bevacizumab for the first-line maintenance treatment of ovarian cancer is not an approved indication.
*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.
BICR = blinded independent central review; BID = twice daily; BRCA = breast cancer susceptibility gene; BRCAm = BRCA mutation; CR = complete response; FIGO = International Federation of Gynecology and Obstetrics; NED = no evidence of disease; OS = overall survival; PFS = progression-free survival; PFS2 = time to second progression; PR = partial response; RECIST = Response Evaluation Criteria in Solid Tumours; TFST = time to first subsequent therapy; TSST = time to second subsequent therapy.

1. Ray-Coquard I, et al. N Engl J Med. 2019;381:2416-28; 2. Ray-Coquard I, et al. Presented at: ESMO; 27 September–1 October 2019; Barcelona, Spain. Abstract LBA2.

Courtesy of Robert L Coleman, MD

PAOLA-1: 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**

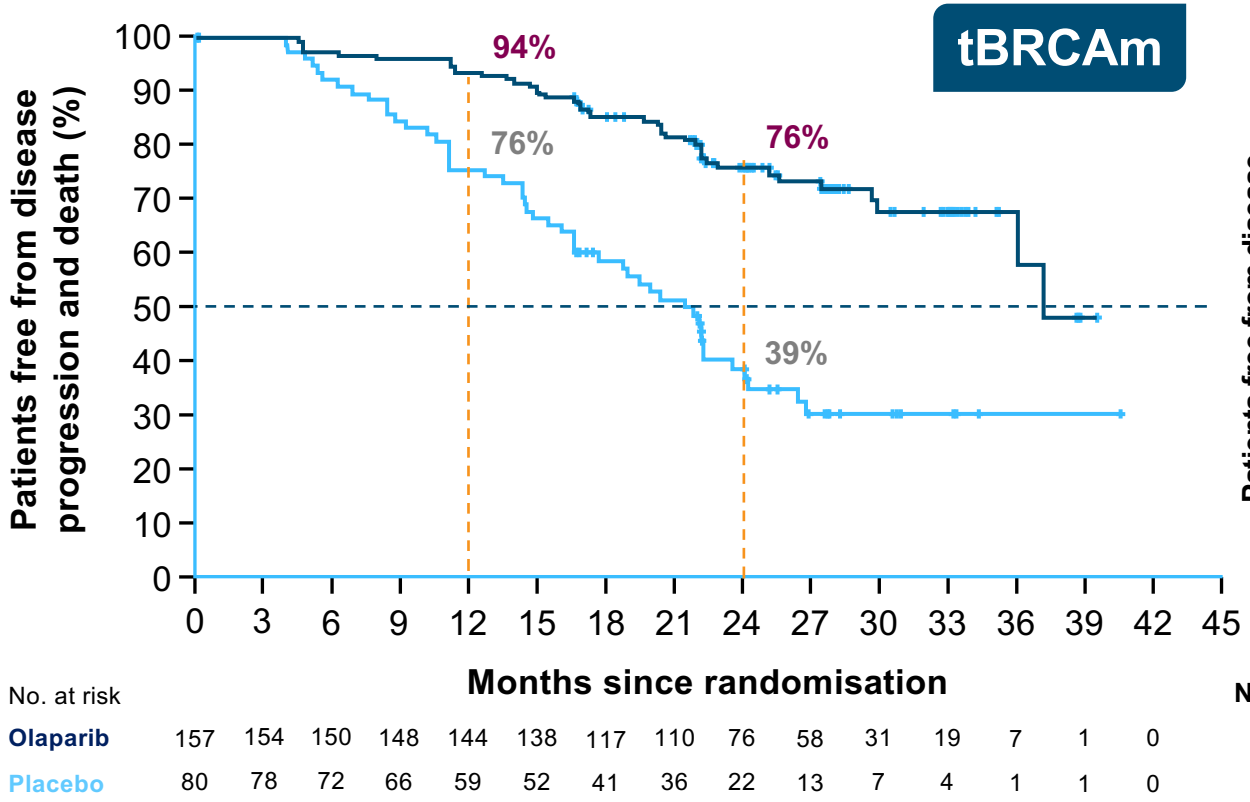
HR 0.59 (95% CI 0.49–0.72; *P*<0.0001)

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

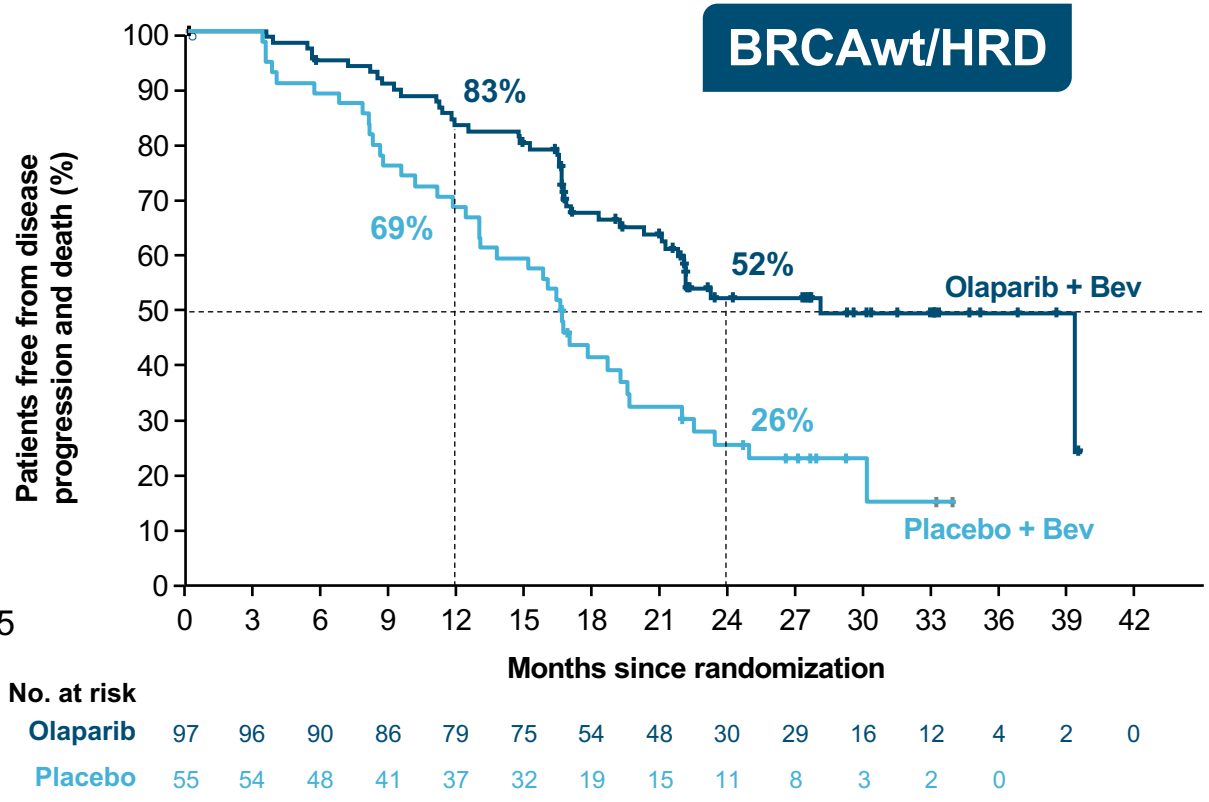
ITT, intent-to-treat population
Ray-Coquard NEM 2019

Courtesy of Robert L Coleman, MD

PAOLA-1: SUBGROUP TREATMENT EFFECTS



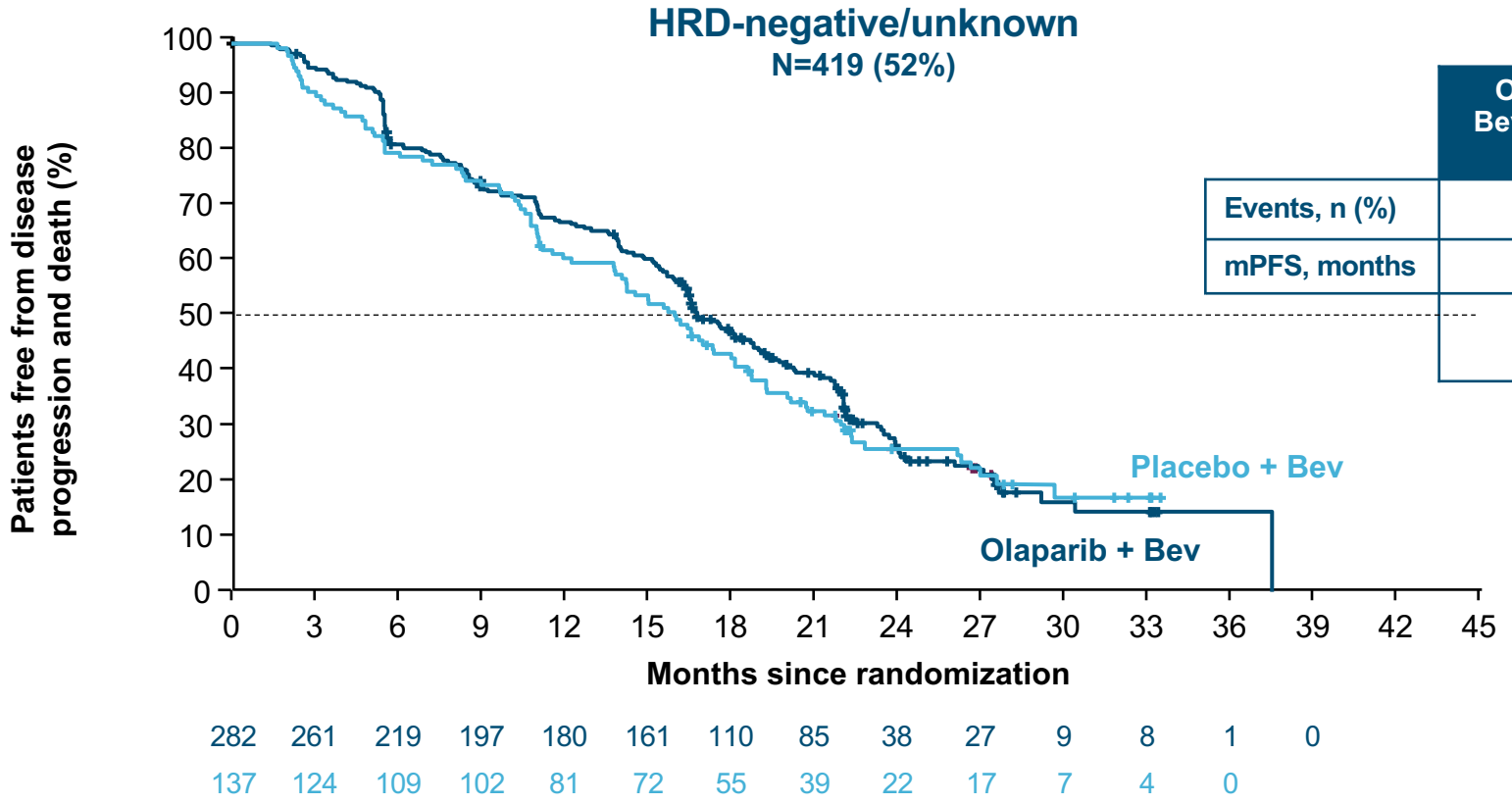
HR 0.31 (95% CI 0.20–0.47)



HR=0.43 95% CI: 0.28, 0.66

Courtesy of Robert L Coleman, MD

PAOLA-1 PFS: HRD-NEGATIVE/UNKNOWN SUBGROUP



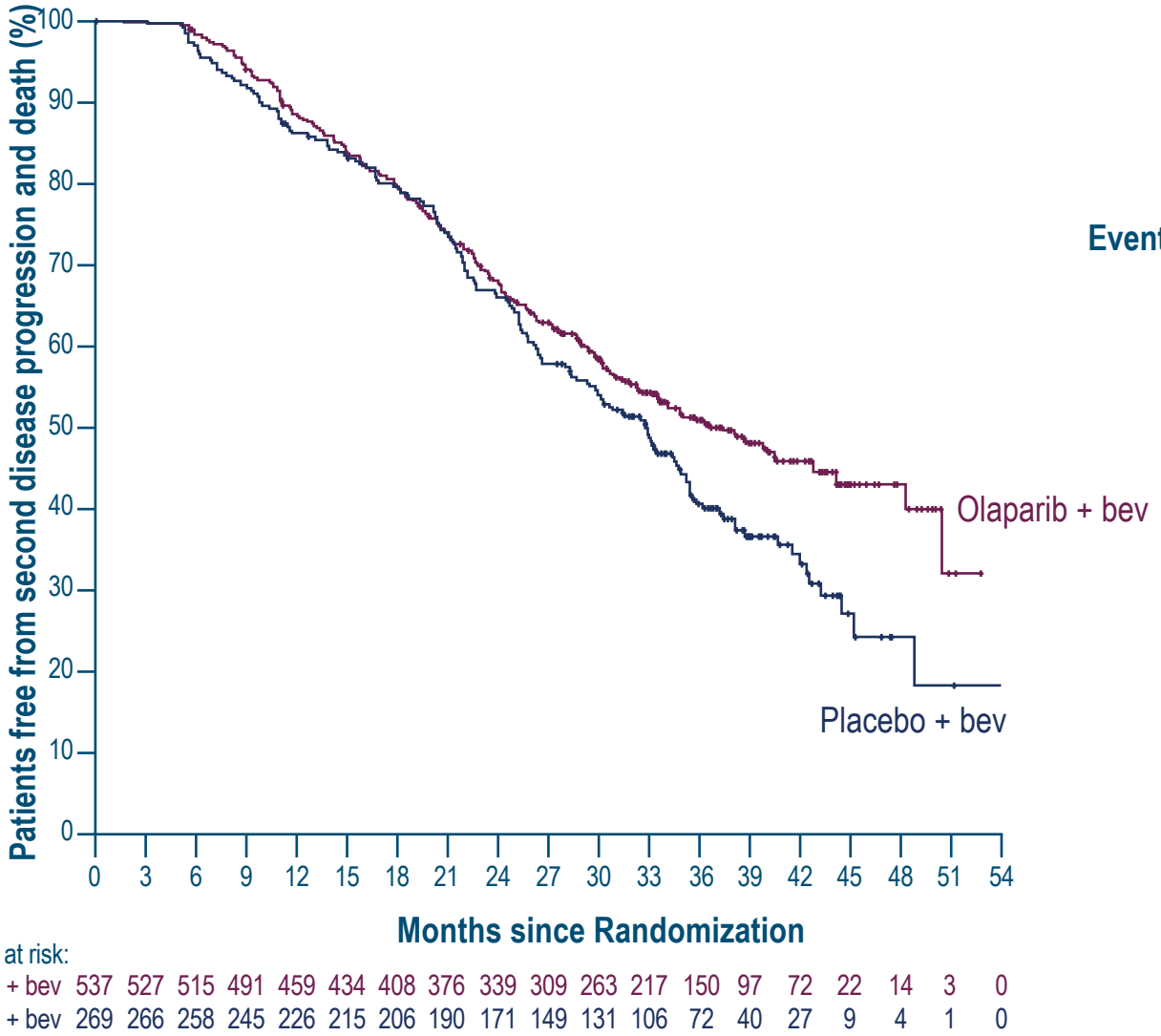
	Olaparib + Bevacizumab (n=282)	Placebo + Bevacizumab (n=137)
Events, n (%)	193 (68)	102 (74)
mPFS, months	16.9	16.0
	HR=0.92 95% CI: 0.72, 1.17	

Subgroup analysis in HRD-negative/unknown population. HRD-positive is an HRD score ≥42.
Addition of olaparib to bevacizumab for the first-line maintenance treatment of ovarian cancer is not an approved indication.
Bev = bevacizumab; HRD = homologous recombination deficiency; PFS=progression-free survival.

1. Ray-Coquard I, et al. N Engl J Med. 2019;381:2416-28; 2. Ray-Coquard I, et al. Presented at: ESMO; 27 September–1 October 2019; Barcelona, Spain. Abstract LBA2.

Courtesy of Robert L Coleman, MD

PAOLA-1: PFS2 (Step-Down Endpoint)



	Olaparib + bev (N=537)	Placebo + bev (N=269)
Events, n (%) [53% maturity]	260 (48)	164 (61)
Median PFS2, months	**36.5**	**32.6**

HR 0.78 (95% CI 0.64–0.95)
***P*=0.0125**

Patients receiving a PARP inhibitor during first subsequent treatment:
Olaparib plus bevacizumab: **9.1%** (49/537)
Placebo plus bevacizumab: **26.8%** (72/269)

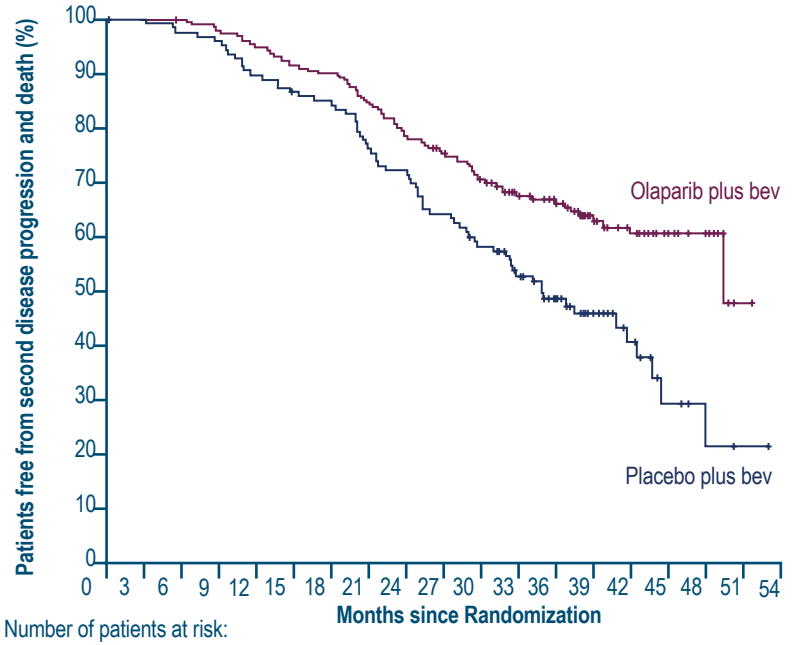
Median PFS2 follow-up of 35.5 months for olaparib plus bevacizumab and 36.5 months for placebo plus bevacizumab

bev, bevacizumab; ITT, intent to treat

Courtesy of Robert L Coleman, MD

PAOLA-1: PFS2 subgroup analysis by HRD status

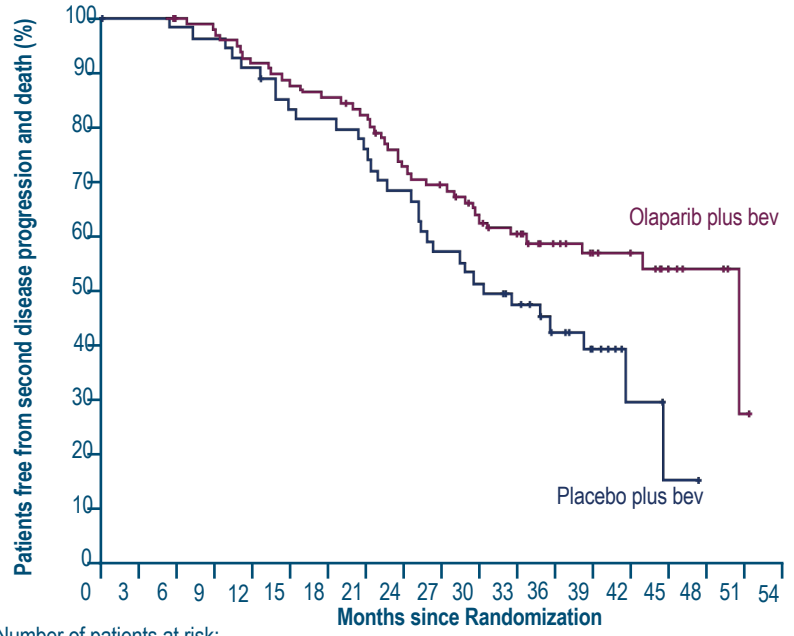
HRD positive,* including tumour BRCAm



	Olaparib + bev (n=255)	Placebo + bev (n=132)
Events, n (%)	85 (33)	70 (53)
Median PFS2, months	**50.3**†	**35.3**

HR 0.56 (95% CI 0.41–0.77)

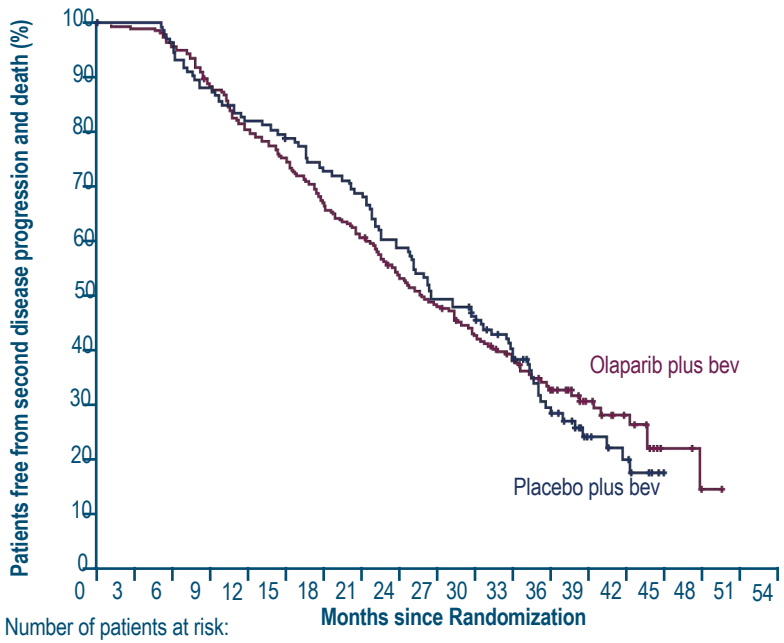
HRD positive,* excluding tumour BRCAm



	Olaparib + bev (n=97)	Placebo + bev (n=55)
Events, n (%)	41 (42)	33 (60)
Median PFS2, months	**50.3**†	**30.1**

HR 0.60 (95% CI 0.38–0.96)

HRD negative/unknown



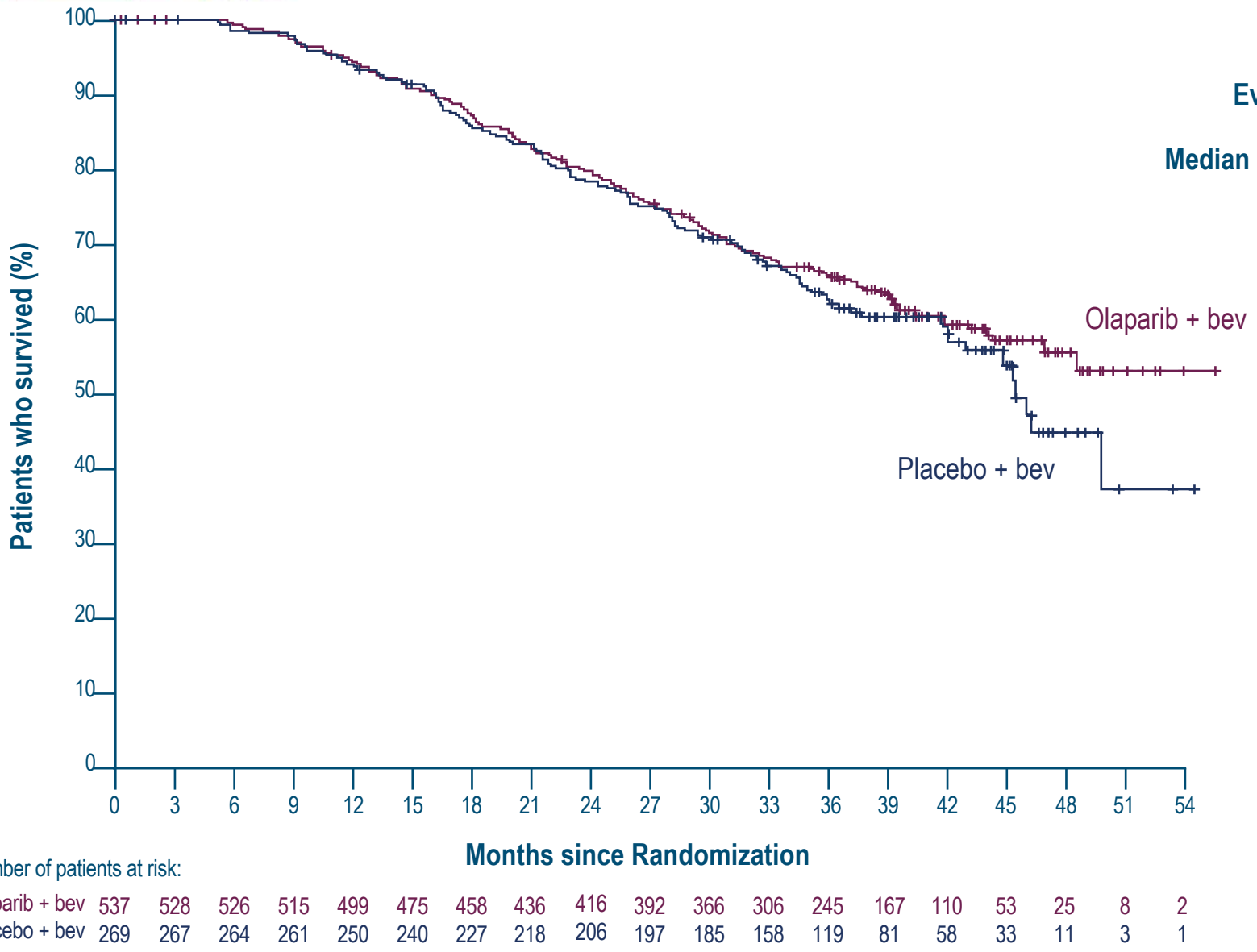
	Olaparib +bev (n=282)	Placebo + bev (n=137)
Events, n (%)	175 (62)	94 (69)
Median PFS2, months	**26.3**	**28.1**

HR 0.98 (95% CI 0.77–1.27)

*HRD positive defined as a tumour BRCAm and/or genomic instability score of ≥42 on the Myriad myChoice CDx® assay; †Unstable median due to lack of events

Courtesy of Robert L Coleman, MD

PAOLA-1: Interim OS analysis



	Olaparib + bev (N=537)	Placebo + bev (N=269)
Events, n (%)	195 (36)	108 (40)
Median OS, months	**NR**	**45.8**

HR 0.93 (95% CI 0.74–1.18)
***P*=0.5631**

- Immature OS analysis:
  - The low event rate (38%) means that definitive conclusions cannot be drawn
- Updated OS data will be presented at greater data maturity:
  - Prespecified final OS analysis planned at ≈60% data maturity or 3 years after primary PFS analysis (March 2022)

NR, not reached

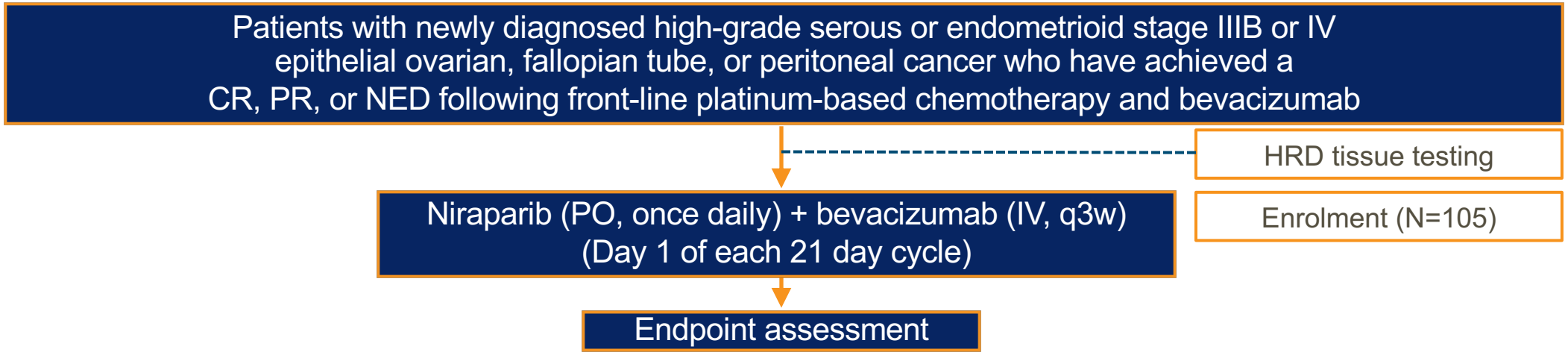
Courtesy of Robert L Coleman, MD

CONCLUSIONS

- Primary endpoint successfully reached (ITT population)
  - Subgroup analyses call to question efficacy in HRD test negative population
- Licensed population is HRD test positive
- PFS2 (step down endpoint) in ITT also positive
  - PFS2 in licensed population suggests efficacy
- OS immature

Courtesy of Robert L Coleman, MD

OVARIO – Trial design and endpoints



Primary endpoint	• Progression-free survival (PFS) rate at 18 months
Key secondary endpoints	• PFS • Overall survival (OS) • Time to first subsequent therapy (TFST) • Time to second subsequent therapy (TSST) • Safety, Incidence of treatment-emergent adverse events (TEAEs) • Functional assessment of cancer therapy – ovarian cancer symptom index (FOSI) • RECIST or CA-125 PFS by RECIST v1.1 per investigator or CA-125 measurement using GCIG criteria
Exploratory endpoints	• PFS rate at 6 and 12 months

Hardesty MM et al. SGO 2020;Abstract 4.

Courtesy of Robert L Coleman, MD

OVARIO – Exploratory endpoints

PFS rates at 6 months and 12 months

Parameter	Overall population (N=105)	HRd (n=49)	HRp (n=38)	HRnd (n=18)
Events at 6 months, n	11	1	7	3
6-month PFS rate, % (95% CI)	90 (82–95)	98 (89–100)	82 (66–92)	83 (59–96)
Events at 12 months, n	26	6	13	7
12-month PFS rate, % (95% CI)	75 (66–83)	88 (75–95)	66 (49–80)	61 (36–83)

- 6- and 12-month PFS efficacy population (N=105) includes all OVARIO patients dosed ≥6 and ≥12 months from data cutoff dates of August 14, 2019, and February 14, 2020, respectively (last patient enrolled February 14, 2019)
- Median follow-up was 8.6 and 12.8 months, respectively

Hardesty MM et al. SGO 2020;Abstract 4.

Courtesy of Robert L Coleman, MD

OVARIO – Overall AEs

Treatment-related TEAEs occurring in ≥10% of patients

Adverse event, n (%)	Any grade (N=105)	Grade ≥3 (N=105)
Thrombocytopenia*	74 (70)	39 (37)
Fatigue	59 (56)	9 (9)
Nausea	54 (51)	1 (1)
Anemia	52 (50)	34 (32)
Hypertension	52 (50)	27 (26)
Proteinuria	40 (38)	3 (3)
Headache	33 (31)	5 (5)
Neutropenia*	29 (28)	13 (12)
Leukopenia*	25 (24)	0 (0)
Epistaxis	19 (18)	0 (0)
Vomiting	16 (15)	1 (1)
Dyspnea	14 (13)	1 (1)
Constipation	13 (12)	0 (0)
Stomatitis	12 (11)	4 (4)
Decreased appetite	12 (11)	0 (0)
Arthralgia	12 (11)	2 (2)

Hardesty MM et al. SGO 2020;Abstract 4.

Courtesy of Robert L Coleman, MD

CONCLUSIONS

- Small phase II demonstrating safety to substitute niraparib for olaparib in a similar design to PAOLA1 experimental arm
- Safety profile similar as well
- Hypothesis generating experiment

Courtesy of Robert L Coleman, MD

Study Design: VELIA/GOG-3005 (NCT02470585)

Patient Population

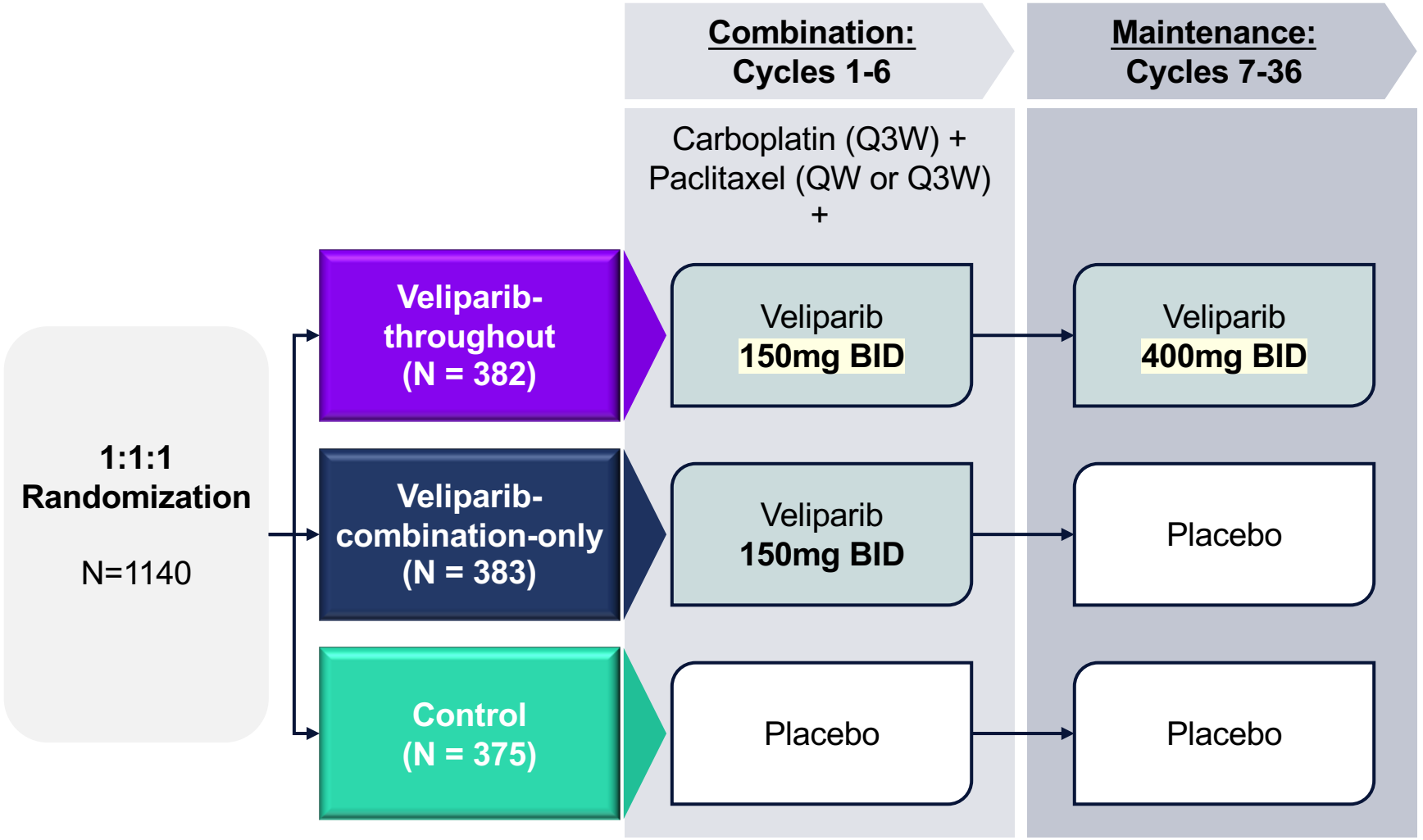
- High-Grade Serous Cancer
- FIGO Stage III or IV
- No Prior Systemic Therapy
- ECOG 0 to 2
- No CNS Metastases

Stratification Factors

- Stage of Disease
- Region
- Primary vs Interval Cytoreduction
- Residual Disease
- Chemotherapy Regimen*
- g*BRCA* Status **

* Carboplatin AUC 6 Q3W + Paclitaxel 80 mg/m^2 QW or 175 mg/m^2 Q3W

** Added as stratification factor ~14 months after trial initiation due to noted imbalance



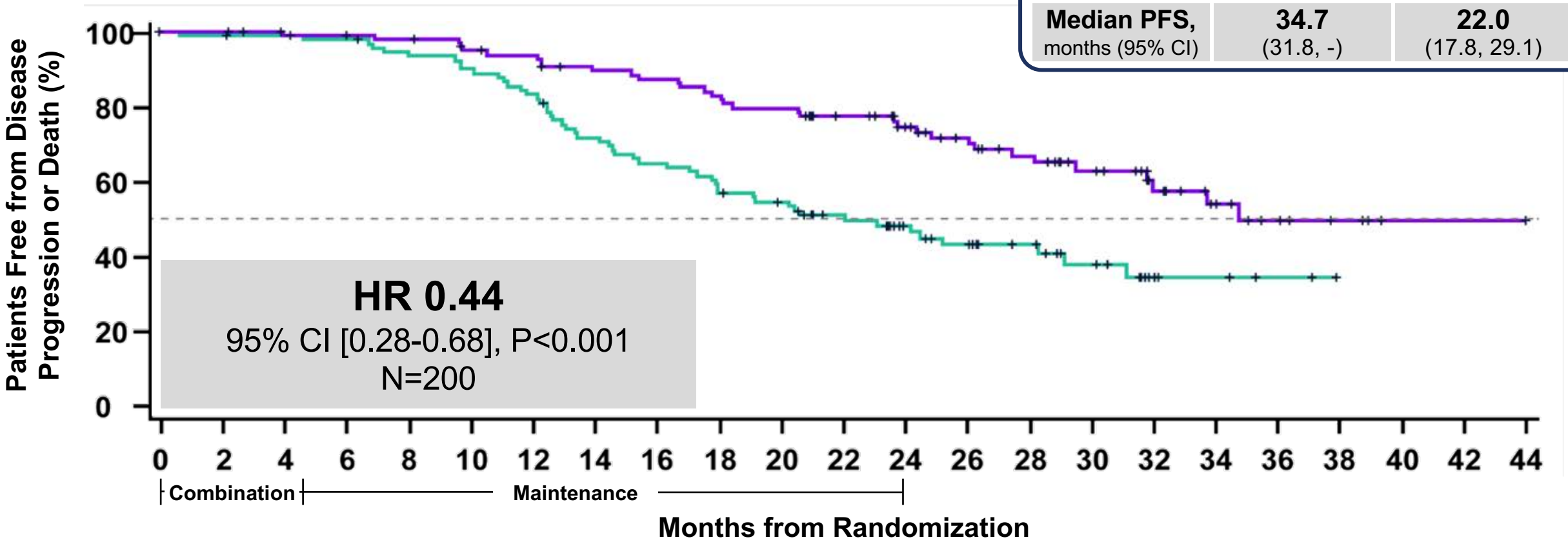
Courtesy of Robert L Coleman, MD

BARCELONA 2019 ESMO congress

VELIA: PFS by Investigator Assessment
*BRCA*m Population

*BRCA*m | HRD | Non-HRD

*BRCA*m	Veliparib-throughout	Control
Events (%)	34/108 (31.5)	51/92 (55.4)
Median PFS, months (95% CI)	**34.7** (31.8, -)	**22.0** (17.8, 29.1)



No. at Risk

Control	92	90	89	88	84	80	74	63	57	50	46	38	29	24	19	13	6	4	2	0	
Veliparib-throughout	108	102	99	97	95	90	88	82	80	76	73	65	53	45	38	30	21	14	9	5	1	1	0

BARCELONA 2019 ESMO congress

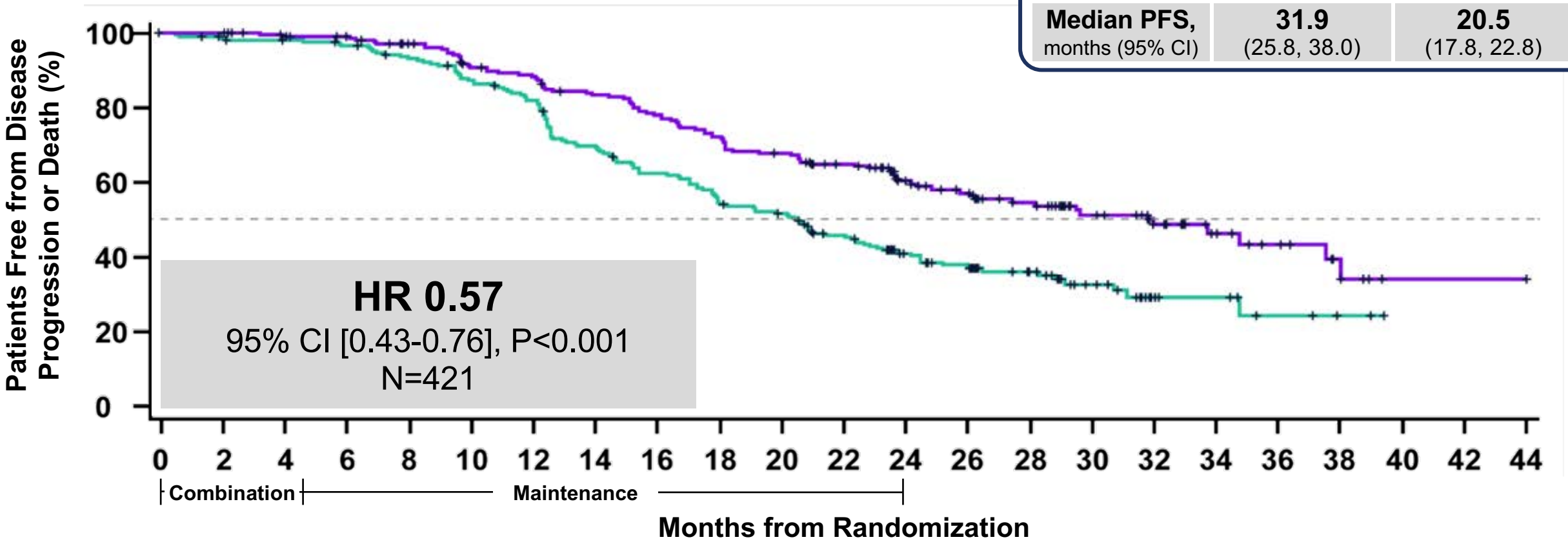
Median duration of follow-up was 28 months at the time of database lock.

Courtesy of Robert L Coleman, MD

VELIA: PFS by Investigator Assessment HRD Population

*BRCA*m HRD | Non-HRD

HRD	Veliparib-throughout	Control
Events (%)	87/214 (40.7)	124/207 (59.9)
Median PFS, months (95% CI)	**31.9** (25.8, 38.0)	**20.5** (17.8, 22.8)



No. at Risk

Control	207	199	196	191	183	170	158	134	119	104	97	79	55	47	34	22	11	9	4	2	0
Veliparib-throughout	214	203	195	191	182	167	161	150	140	130	121	109	82	72	58	44	30	19	14	5	1	1	0

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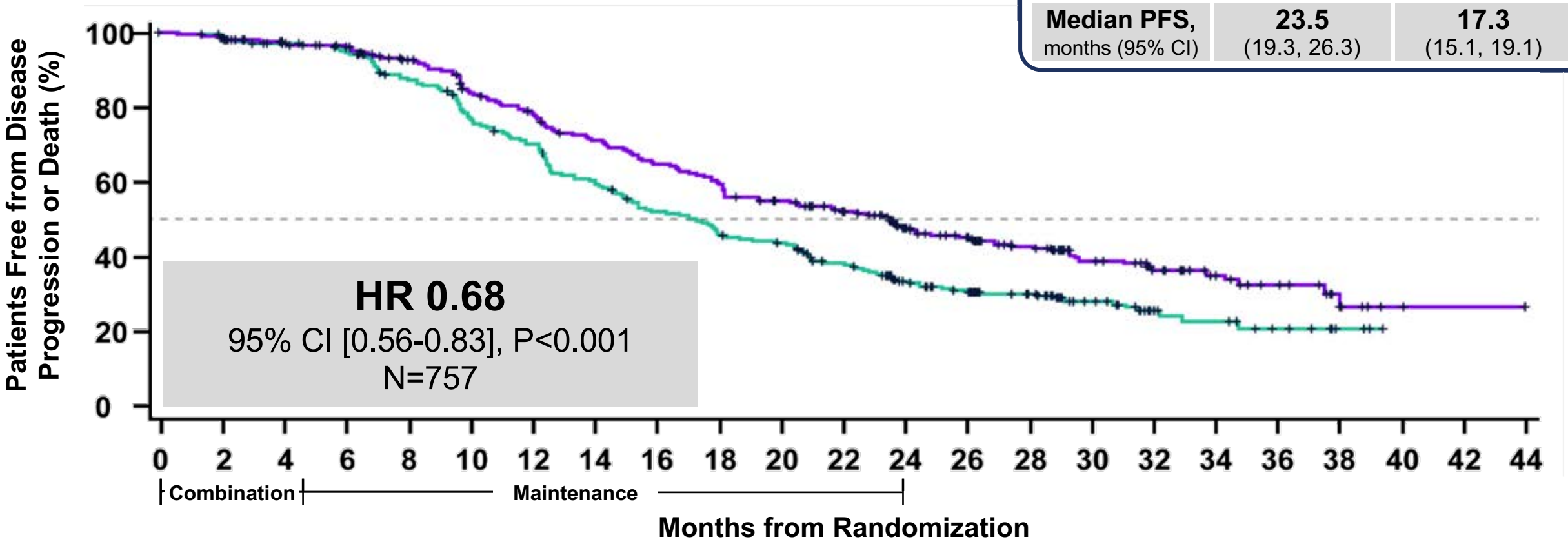
Median duration of follow-up was 28 months at the time of database lock.

Courtesy of Robert L Coleman, MD

VELIA: PFS by Investigator Assessment ITT Population

***BRCA*m** | **HRD** | **Non-HRD**

ITT	Veliparib-throughout	Control
Events (%)	191/382 (50.0)	237/375 (63.2)
Median PFS, months (95% CI)	**23.5** (19.3, 26.3)	**17.3** (15.1, 19.1)



No. at Risk

Control	375	356	340	328	297	260	236	202	172	153	143	119	84	70	55	36	21	16	10	3	0
Veliparib-throughout	382	352	337	329	308	275	253	228	208	192	172	153	111	95	76	55	38	26	19	7	2	1	0

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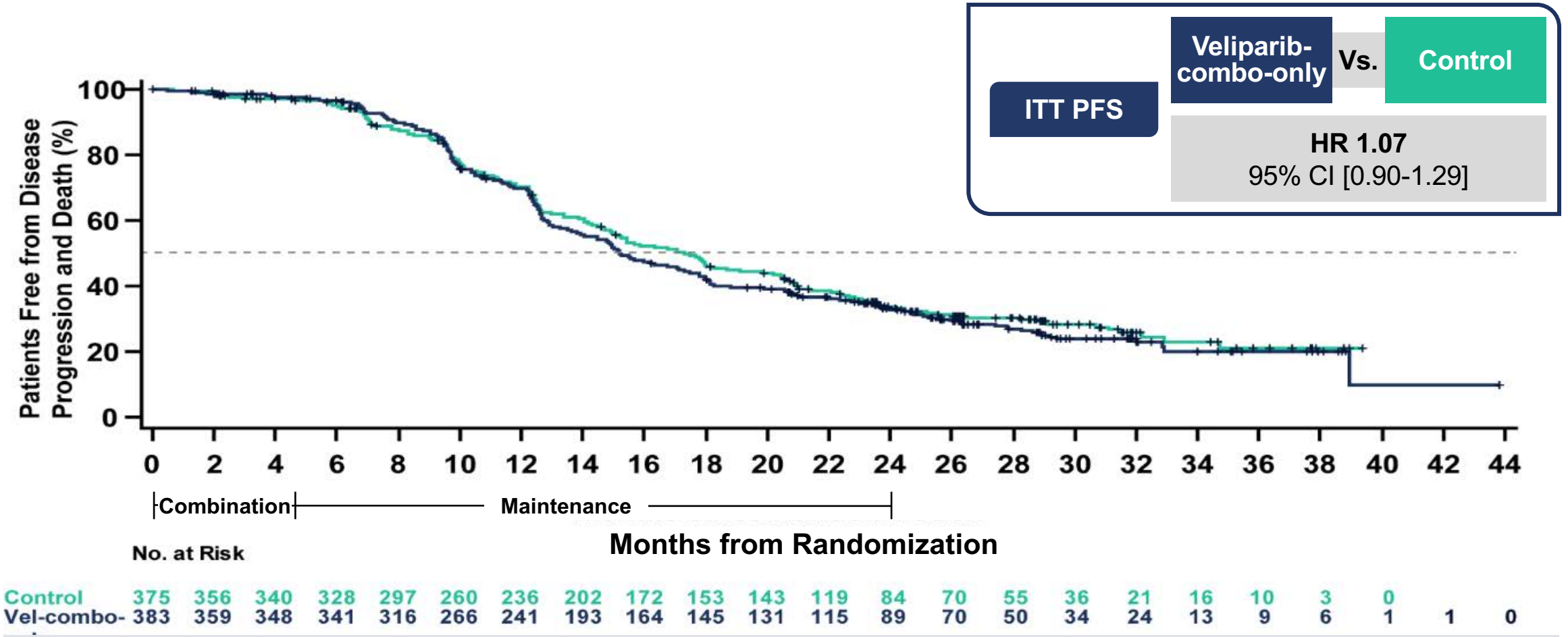
Median duration of follow-up was 28 months at the time of database lock.

Courtesy of Robert L Coleman, MD

VELIA: PFS for Veliparib-combo-only vs. Control



Across *BRCA*m, HRD, and ITT, the veliparib-combo-only arm and the control arm demonstrated similar PFS

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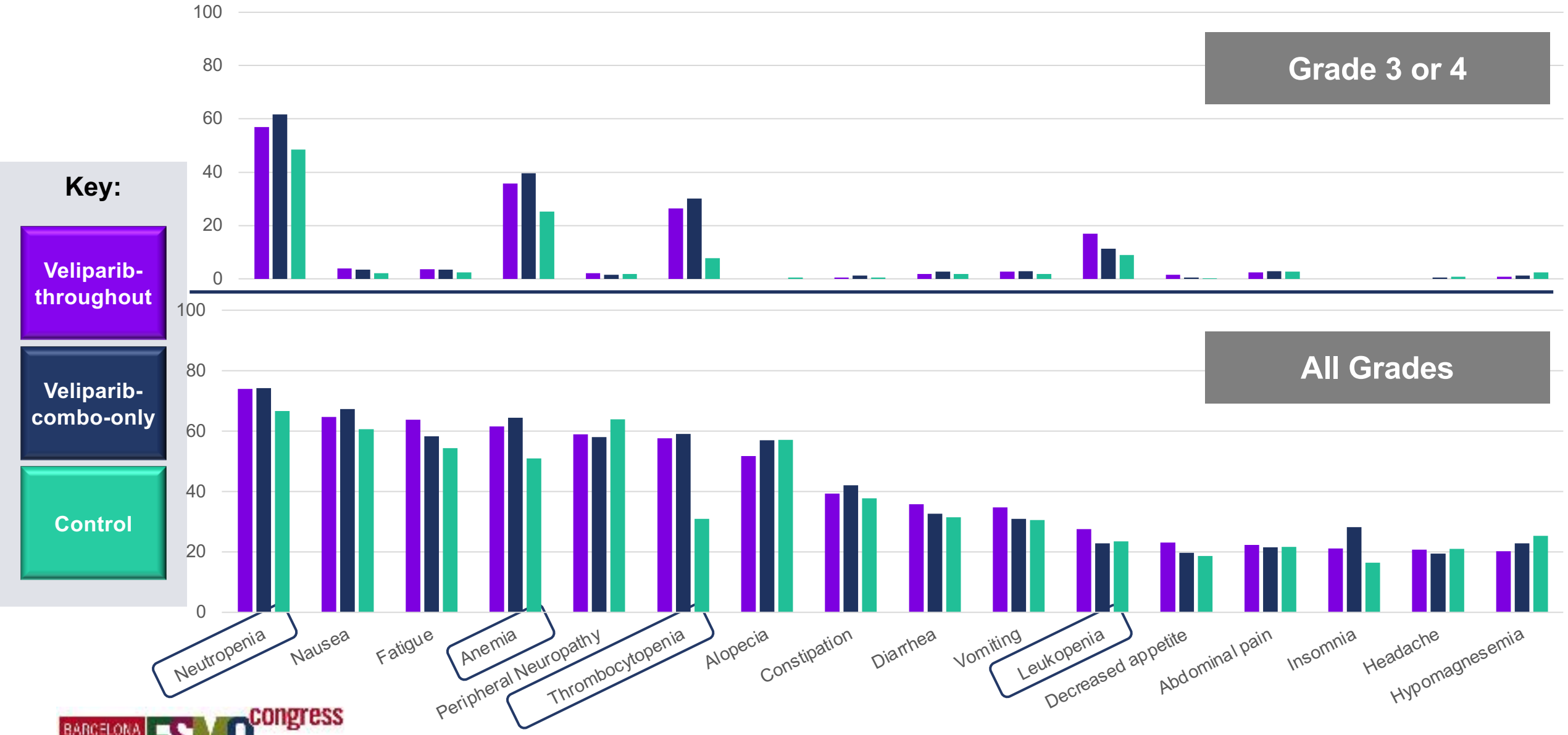
Courtesy of Robert L Coleman, MD

VELIA: Adverse Events — Combination Phase (Cycles 1-6)



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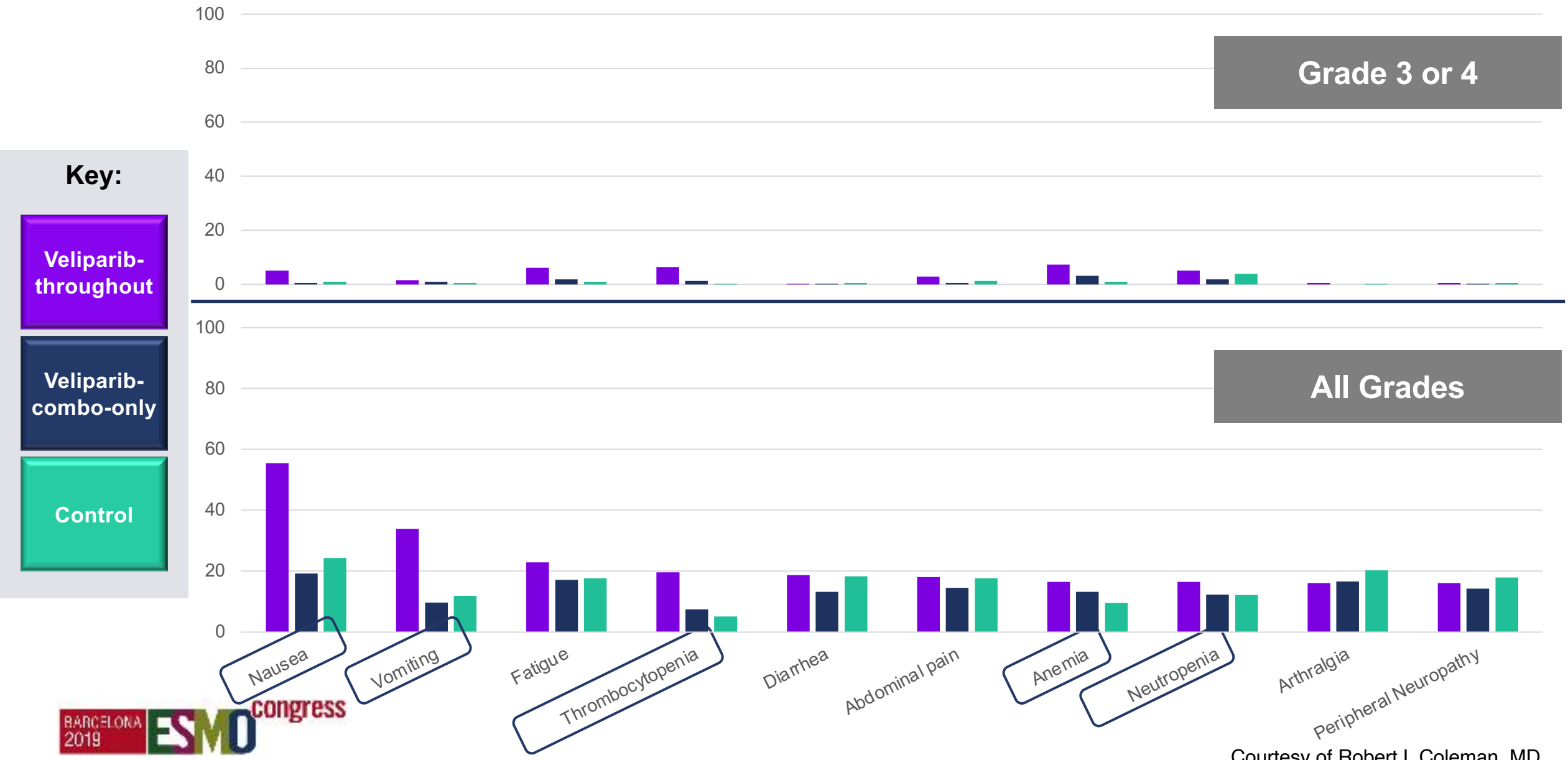
Courtesy of Robert L Coleman, MD

VELIA: Adverse Events — Maintenance Phase (Cycles 7-36)



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Courtesy of Robert L Coleman, MD

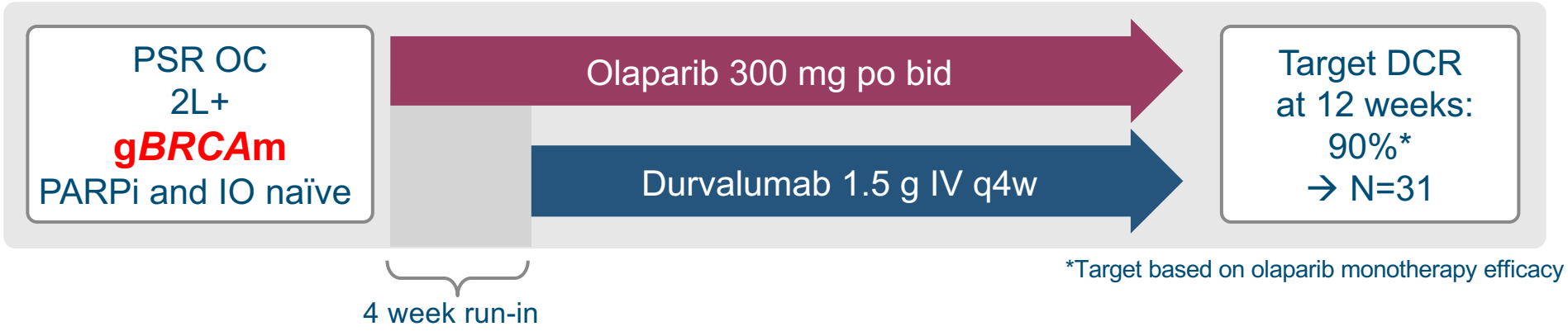
CONCLUSIONS

- VELIA successfully met all primary endpoints from step-down analyses
- Safety largely consistent with independent effects of PARPi and chemotherapy
- Support for PARPi therapy during chemotherapy questioned by small impact from combination (no maintenance) vs chemotherapy

Courtesy of Robert L Coleman, MD

MEDIOLA

Initiation of therapy at the time of relapse



- Primary endpoints: DCR at 12 weeks, safety
- Secondary endpoints: DCR at 28 weeks, ORR, DoR, PFS, OS, PD-L1 expression
- Exploratory endpoints: TILs

DCR, disease control rate; DoR, duration of response; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; po, oral; TILs, tumor-infiltrating lymphocytes

Lancet Onc 2020

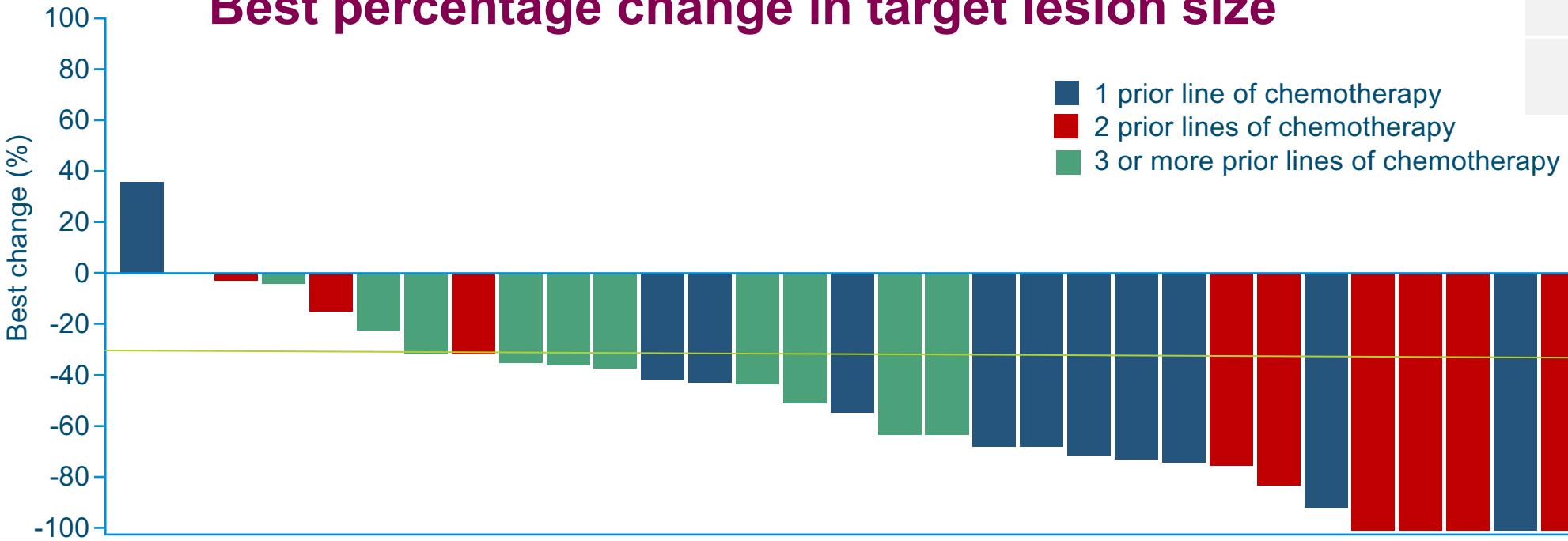
Courtesy of Robert L Coleman, MD

MEDIOLA: Tumor responses

	1 prior (2L)	2 prior (3L)	3+ prior (4L)	All lines
ORR	10/13=**77%**	6/9=**67%**	7/10=**70%**	23/32=**72%**
95% CI	(46%, 95%)	(30%, 93%)	(35%, 93%)	(53%, 86%)

Best Response	N (%)
CR	**6 (19)**
PR	**17 (53)**
SD	3 (9)
PD	3 (9)
NE	3 (9)

Best percentage change in target lesion size



Drew Y SGO 2018

Courtesy of Robert L Coleman, MD

VIRTUAL ESMO congress 2020

Phase II study of olaparib plus durvalumab and bevacizumab (MEDIOLA): initial results in patients with non-germline BRCA-mutated platinum sensitive relapsed ovarian cancer

Yvette Drew,[1] Richard Penson,[2] David M O'Malley,[3] Jae-Weon Kim,[4] Stefan Zimmermann,[5] Patricia Roxburgh,[6] Joohyuk Sohn,[7] Salomon M Stemmer,[8] Sara Bastian,[9] Michelle Ferguson,[10] Benoit You,[11] Susan Domchek,[12] Haiyan Gao,[13] Helen K Angell,[13] Kassondra Meyer,[14] Laura Opincar,[14] Lone Ottesen,[13] Susana Banerjee[15]

[1]Northern Centre for Cancer Care, Newcastle upon Tyne Hospitals NHS Foundation Trust, and Newcastle University, Newcastle upon Tyne, UK; [2]Massachusetts General Hospital, Boston, MA, USA; [3]The Ohio State University – James Comprehensive Cancer Center, Columbus, OH, USA; [4]Seoul National University Hospital, Seoul, Republic of Korea; [5]Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland; [6]Beatson West of Scotland Cancer Centre, and Institute of Cancer Sciences, University of Glasgow, Glasgow, UK, [7]Yonsei Cancer Centre, Yonsei University, Sinchon-dong, Republic of Korea; [8]Rabin Medical Center-Beilinson Campus, Petach Tikva and Tel-Aviv University, Tel-Aviv, Israel; [9]Kantonsspital Graubuenden, Chur, Switzerland; [10]NHS Tayside, Dundee, UK; [11]Institut de Cancérologie des Hospices Civils de Lyon, CITOHL, GINECO, Université Claude Bernard Lyon 1, Lyon, France; [12]Basser Center for BRCA University of Pennsylvania, Philadelphia, PA, USA; [13]AstraZeneca, Cambridge, UK; [14]AstraZeneca, Gaithersburg, MD, USA; [15]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK

ClinicalTrials.gov identifier: NCT02734004

Plain-language summary

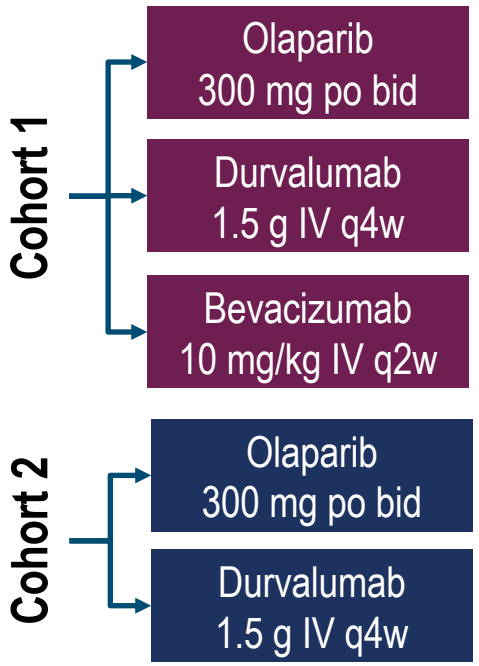
esmo.org

Courtesy of Robert L Coleman, MD

MEDIOLA: gBRCAwt cohorts
Study schema and patient demographics

Patient population

- gBRCAwt
- PSR ovarian cancer
- ≤2 prior lines of chemotherapy
- PARP inhibitor and IO agent naïve



Treatment to disease progression

Primary endpoints

- DCR at 24 weeks (target 80%)
- Safety and tolerability

Secondary endpoints include:

- DCR at 56 weeks, ORR, DOR, PFS, OS, PK

Exploratory endpoints:

- Tumour genetics and immunology biomarkers

Sequential enrolment

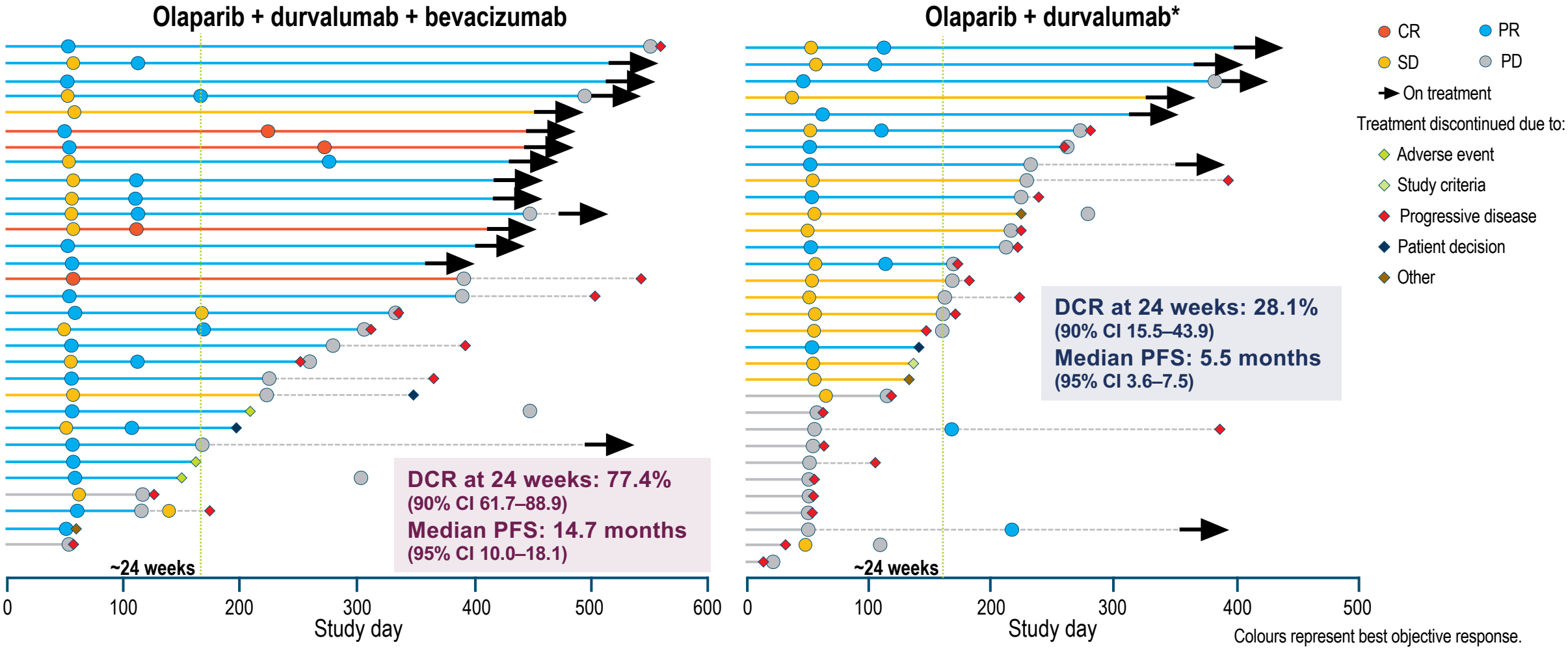
Tumour assessments every 8 weeks

	Olap + durva + bev (N=31)	Olap + durva (N=32)
Median age, years	64.0	68.5
Age group (years), n (%)		
<50	3 (9.7)	4 (12.5)
≥50–<65	14 (45.2)	8 (25.0)
≥65	14 (45.2)	20 (62.5)
Race, n (%)		
White	20 (64.5)	24 (75.0)
Asian	10 (32.3)	3 (9.4)
Other	1 (3.2)	5 (15.6)
Platinum sensitivity, n (%)		
>6–12 months	18 (58.1)	14 (43.8)
>12 months	13 (41.9)	18 (56.3)
Number of prior lines of chemotherapy, n (%)		
1 prior line	20 (64.5)	23 (71.9)
2 prior lines	11 (35.5)	9 (28.1)

Bid, twice daily; DCR, disease control rate; DOR, duration of response; IO, immuno-oncology; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; po, by mouth; PSR, platinum-sensitive relapsed; q2w, every 2 weeks; q4w, every 4 weeks

Courtesy of Robert L Coleman, MD

MEDIOLA: Time to progression or treatment discontinuation
Triplet cohort showed high DCR at 24 weeks and long median PFS



Colours represent best objective response.

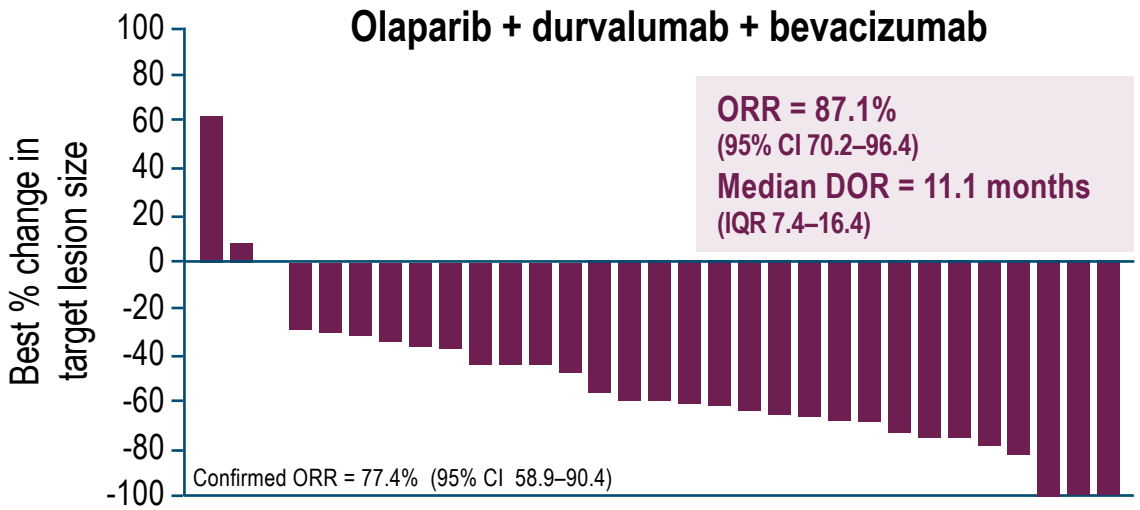
*Four patients had out of window (±1 week) scans at week 24, and were counted as not evaluable for DCR, despite having SD or PR before and after week 24

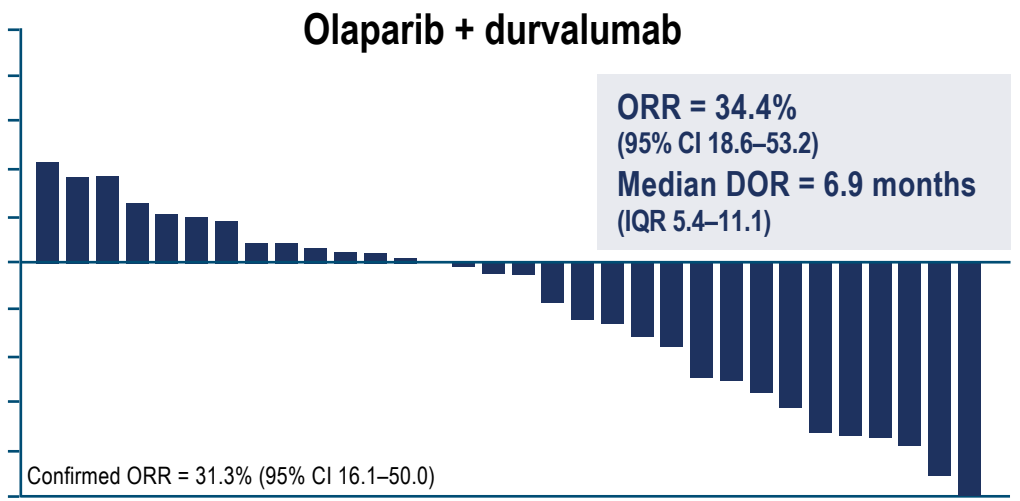
CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease

Drew Y et al. ESMO 2020;Abstract 814MO.

Courtesy of Robert L Coleman, MD

MEDIOLA: Triplet cohort demonstrates high ORR
Exploratory analysis suggests triplet cohort ORR is not GIS-dependent





Genomic instability status* subgroup	Olaparib + durvalumab + bevacizumab		Olaparib + durvalumab	
	ORR (95% CI), %	n/N patients	ORR (95% CI), %	n/N patients
GIS-positive	100.0 (69.2–100.0)	10/10	50.0 (18.7–81.3)	5/10
GIS-negative	**75.0 (34.9–96.8)**	**6/8**	**16.7 (0.4–64.1)**	**1/6**
GIS-unknown	84.6 (54.6–98.1)	11/13	31.3 (11.0–58.7)	5/16

*GIS, as determined by Foundation Medicine tumour analysis; must have genome-wide LOH ≥14, a somatic *BRCA1* and/or *BRCA2* mutation, or a mutation in *ATM*, *BRIP1*, *PALB2*, *RAD51C*, *BARD1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PPP2R2A*, *RAD51B*, *RAD51D* or *RAD54L* to be considered positive. At the time of the DCO, the prespecified cut-off for genome-wide LOH of 14% was used[1]; GIS, genomic instability status; IQR, interquartile range; LOH, loss of heterozygosity. [1]Swisher *et al. Lancet Oncol* 2017;18:75–87

Drew Y et al. ESMO 2020;Abstract 814MO.

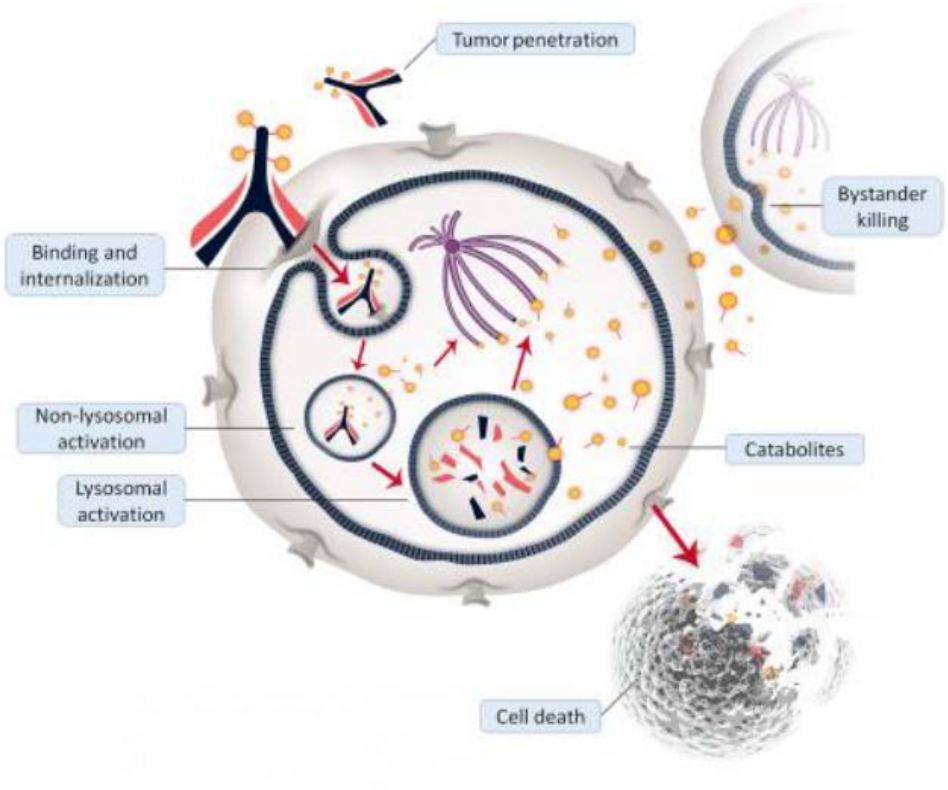
Courtesy of Robert L Coleman, MD

Conclusions

- The triplet combination of olaparib, durvalumab and bevacizumab showed promising efficacy as treatment in the absence of chemotherapy for women with germline BRCA wildtype platinum-sensitive relapsed advanced ovarian cancer, with 77% DCR at 24 weeks and median PFS of 15 months
- Exploratory analysis suggests the high ORR in the triplet cohort was not driven by differences in genomic instability status; ORR was ≥75% in the GIS+, GIS− and GIS unknown subgroups
- The safety profile of the combination of olaparib plus durvalumab with or without bevacizumab was consistent with the known safety profiles expected for the single agents
- The combination of olaparib, durvalumab and bevacizumab is now being tested as part of first-line **maintenance** treatment in the Phase III study, DUO-O (NCT03737643)

Courtesy of Robert L Coleman, MD

Mirvetuximab Soravtansine (MIRV) In Combination With Bevacizumab In Patients With Platinum Agnostic Ovarian Cancer



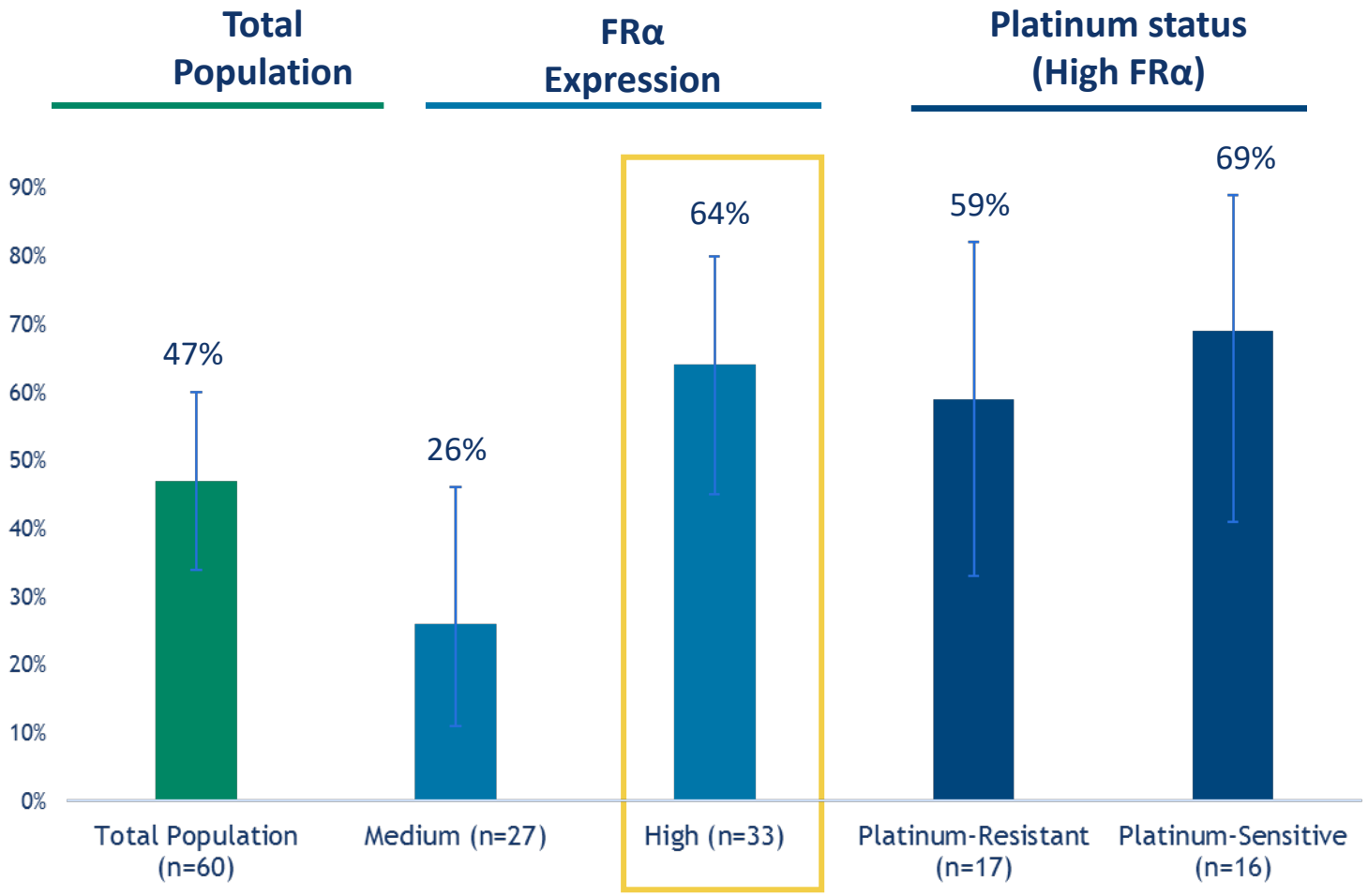
Enrolled patients with folate receptor medium to high expressing tumors
Allowed both plat sens and plat resistant tumors

Characteristic	N=60
Age (median)	60 (44-83)
ECOG PS	
0	75%
1	25%
# prior therapies	
1	33%
2	37%
≥3	30%
FR alpha	
med	45%
high	55%
Prior regimens	
Platinums	100%
Taxanes	98%
Bevacizumab	40%
PARPi	32%
Platinum Free Interval	
< 6 months	53%
6-12 months	33%
> 12 months	13%

Courtesy of Robert L Coleman, MD

Gilbert et al. ASCO 2020 (virtual) Chicago Abstract 6004

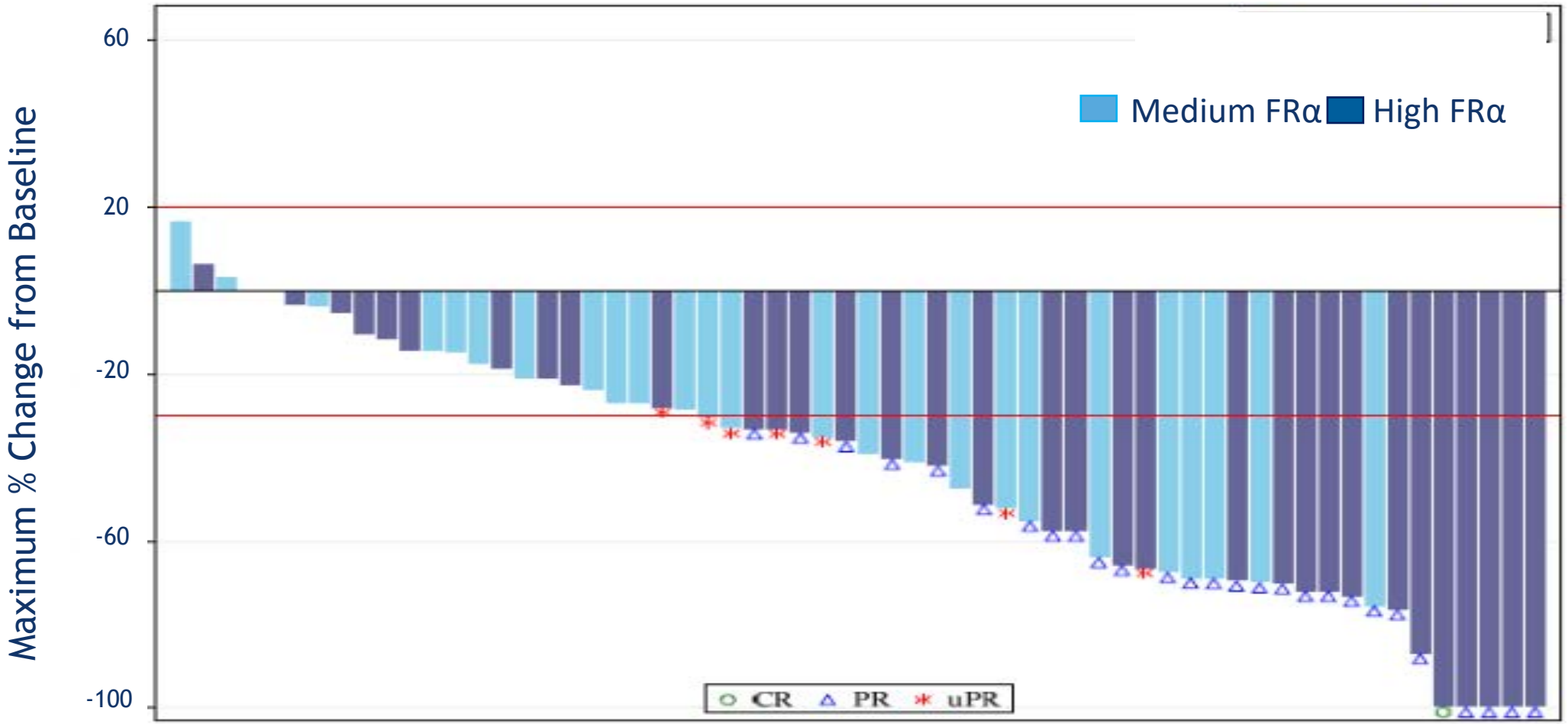
ORR by FRα Expression and Platinum Status with MIRV/Bev



- 47% ORR (28/60) for overall cohort
- 64% ORR (21/33) in high FRα pts
  - 59% ORR (10/17) in-platinum-resistant subset
  - 69% ORR (11/16) in platinum-sensitive subset
- With a median follow-up of 8.5 months, the duration of response and progression free survival data are immature

Courtesy of Robert L Coleman, MD

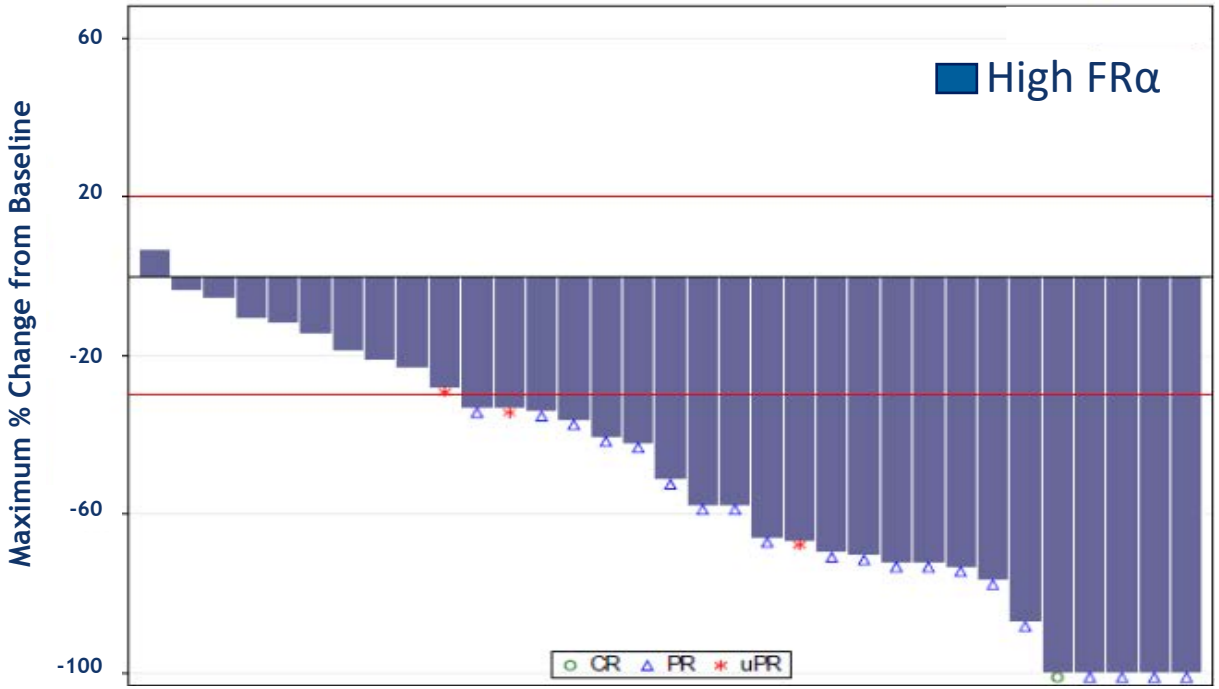
Maximum Tumor Change (%) in Target Lesions from Baseline with MIRV/Bev

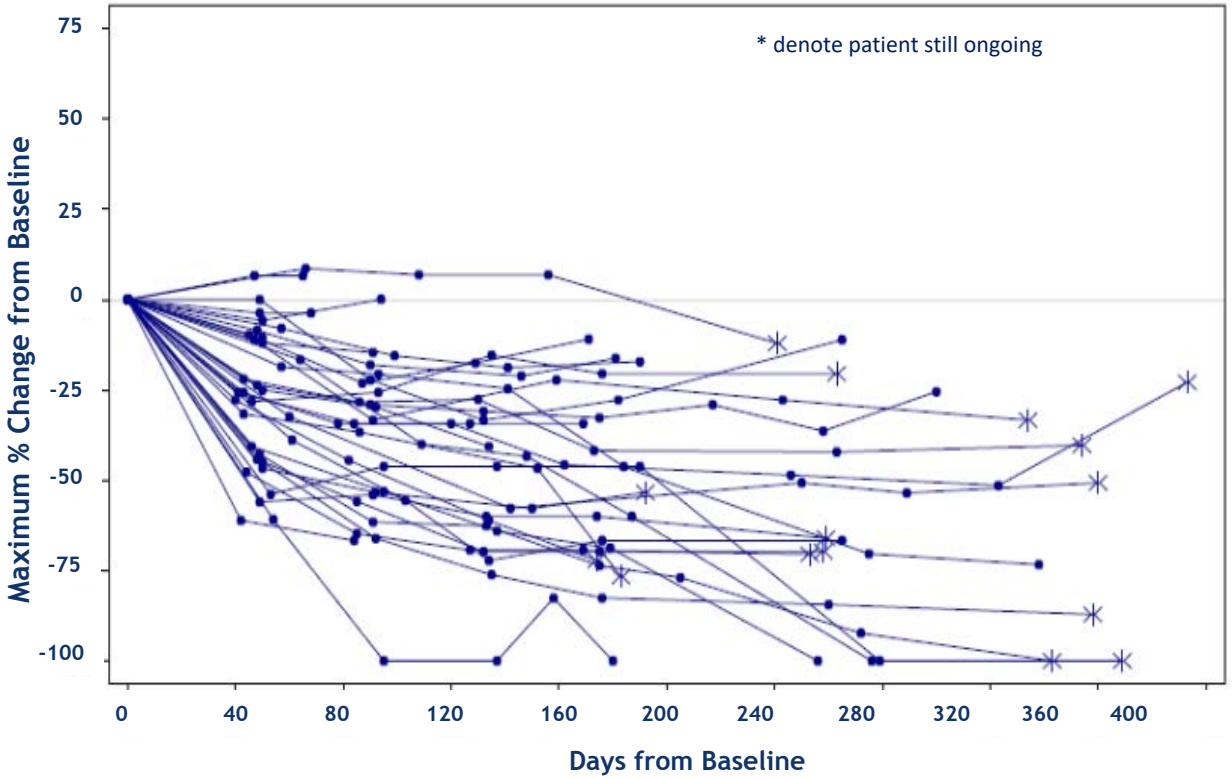


- 92% (55/60) of patients demonstrated tumor reduction
- Deeper tumor responses in high FRα pts

Courtesy of Robert L Coleman, MD

Depth and Duration of Tumor Reduction with MIRV/Bev in High FRα Patients





- More durable tumor reductions in high FRα, with 46% of high FRα (vs 26% of medium FRα) remaining on treatment
- With a median duration of follow-up of 8.5 months, duration of response (DOR) and progression free survival (PFS) are immature

Courtesy of Robert L Coleman, MD

CONCLUSIONS

- Mirvetuximab soravtansine combines well with bevacizumab
- The adverse events observed were manageable, and consistent with the side effect profiles of each agent
- The clinical activity is consistent with previously reported mirvetuximab plus bevacizumab data demonstrating greater depth and duration of response in high FRα tumors
- The combination of mirvetuximab soravtansine and bevacizumab may benefit an increasing population of recurrent ovarian cancer for whom a non-platinum based regimen would be appropriate providing a potential development option

Courtesy of Robert L Coleman, MD

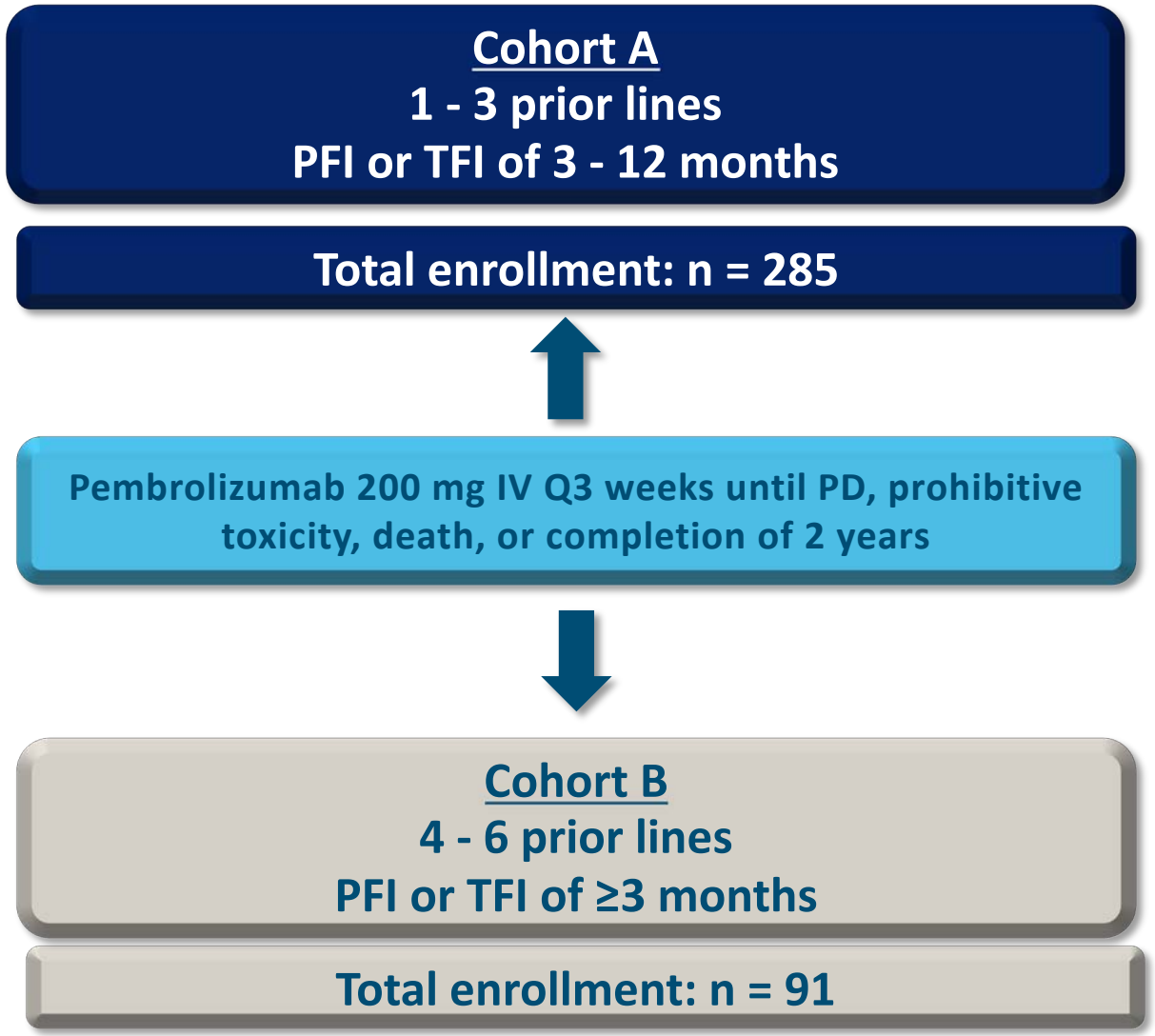
KEYNOTE-100 (NCT02674061): Phase 2, Two-Cohort Study of Pembrolizumab for Recurrent Advanced Ovarian Cancer

Patients (N = 376)

- Recurrent, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer
- ECOG PS 0 or 1
- Provision of a tumor sample for biomarker analysis

Key exclusion criteria:

- Mucinous histology
- No bowel obstruction within 3 months
- No active autoimmune disease
- No active CNS metastases and/or carcinomatous meningitis



Courtesy of Robert L Coleman, MD

Matulonis UA, et al. J Clin Oncol. 2018;36(15)5511.; Lederman JA, et al. Ann Oncol. 2018;29(8):vii728.; Matulonis UA, et al. SGO 2019; Abstract 26.; Matulonis UA, et al. Ann Oncol. 2019;30(7)L1080-1087.

KEYNOTE-100: Endpoints and Assessments

- Primary endpoints: ORR per RECIST v1.1 by BICR
  - By cohort
  - By PD-L1 expression level
    - Combined positive score (CPS), defined as the number of PD-L1–positive cells (tumor cells, lymphocytes, and macrophages) out of the total number of tumor cells x 100, was used to determine PD-L1 expression from archival tumor tissue biopsy
    - PD-L1 cut points determined by analyzing ORR data from the first 100 patients enrolled in Cohort A (training set)
- Secondary endpoints: Duration of response, DCR, PFS, OS, safety
- Exploratory endpoints: Biomarker analyses (GEP, WES [HRD,BRCA], CA 125)
- Response assessment: Every 9 weeks after study entry until week 54 and every 12 weeks thereafter until progressive disease, death, or study completion

Matulonis UA et al. ASCO 2020;Abstract 6005.

Courtesy of Robert L Coleman, MD

KEYNOTE-100: Baseline Characteristics

Characteristic, n (%)	N = 376
Age, median (range), y	61 (25 - 89)
<65 years	140 (37)
ECOG performance status	
0	242 (64)
1	134 (36)
Histology	
High-grade serous	283 (75)
Endometrioid	28 (7)
Low-grade serous	21 (6)
Clear cell	19 (5)
Other*	25 (7)

Characteristic, n (%)	N = 376
Number of lines of prior therapy	
1	85 (23)
2	121 (32)
3	79 (21)
4	42 (11)
≥5	49 (13)
PFI/TFI	
1 - 3 months	41 (11)
3 - 6 months	156 (41)
6 - 12 months	143 (38)
>12 months	36 (10)

*Not specified as low- or high-grade serous or listed as papillary serous (n = 12); unclassified or listed as adenocarcinoma or carcinoma (n = 12); transitional (n = 1).
Database cut-off date: September 18, 2019.

Matulonis UA et al. ASCO 2020;Abstract 6005.

Courtesy of Robert L Coleman, MD

KEYNOTE-100: Antitumor Activity — Confirmed Objective Response Rate Based on RECIST v1.1 per BICR

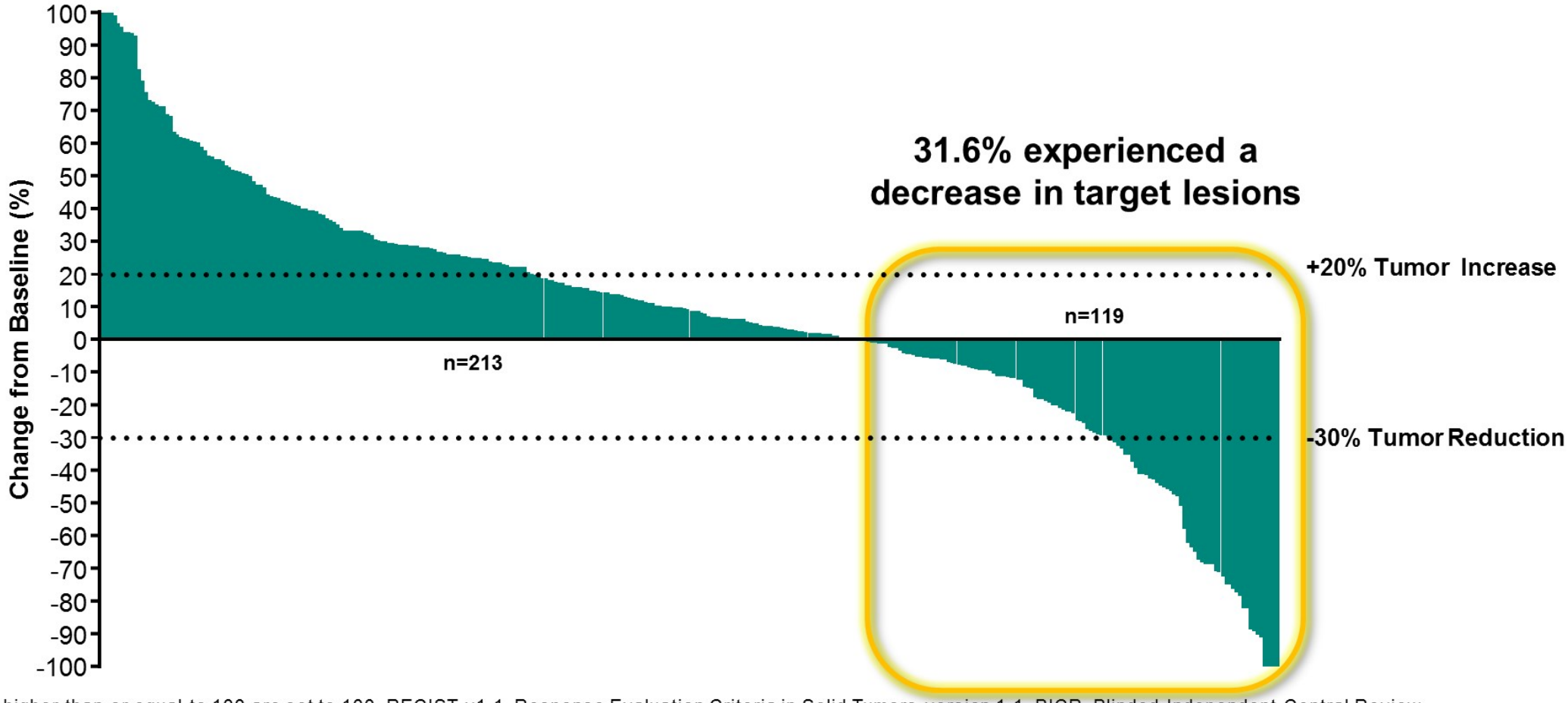
	Cohort A 1 - 3 prior lines; PFI/TFI 3 - 12 months n = 285	Cohort B 4 - 6 prior lines; PFI/TFI ≥3 months n = 91	Cohorts A + B All-comers n = 376
ORR % (95% CI)	**8.1 (5.2 - 11.9)**	**9.9 (4.6 - 17.9)**	**8.5 (5.9 - 11.8)**
DCR % (95% CI)	22.1 (17.4 - 27.4)	22.0 (14.0 - 31.9)	22.1 (18.0 - 26.6)
Best overall response			
Complete response n (%)	5 (1.8)	2 (2.2)	7 (1.9)
Partial response n (%)	18 (6.3)	7 (7.7)	25 (6.6)
Stable disease n (%)	84 (29.5)	25 (27.5)	109 (29.0)
Progressive disease n (%)	165 (57.9)	49 (53.8)	214 (56.9)
Responders (n)	23	9	32
Time to response, median months (range)	2.1 (1.9 - 6.3)	2.1 (1.8 - 12.3)	2.1 (1.8 - 12.3)
Duration of response, median months (range)	8.3 (3.9 - 35.4+)	23.6 (3.3+ - 32.8+)	10.2 (3.3+ - 35.4+)

RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1. BICR, Blinded Independent Central Review. DCR = CR + PR + SD ≥24 weeks.
Database cut-off date: September 18, 2019.

Matulonis UA et al. ASCO 2020;Abstract 6005.

Courtesy of Robert L Coleman, MD

KEYNOTE-100: Best Change from Baseline in Tumor Size in Cohorts A + B — Based on RECIST v1.1 per BICR



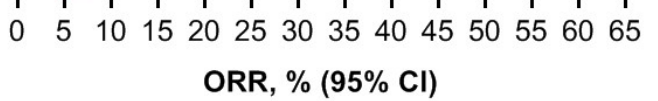
Values higher than or equal to 100 are set to 100. RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1. BICR, Blinded Independent Central Review.
All Subjects as Treated Population. Database cut-off date: September 18, 2019.

Courtesy of Robert L Coleman, MD

Matulonis UA et al. ASCO 2020;Abstract 6005.

KEYNOTE-100: Objective Response Rate by Subgroup

Subgroup	N	ORR, % (95% CI)
Overall	376	8.5 (5.9-11.8)
Age		
<65	236	7.2 (4.3-11.3)
≥65	140	10.7 (6.1-17.1)
Prior Lines of Therapy		
1	85	10.6 (5.0-19.2)
2	121	9.1 (4.6-15.7)
3+	170	7.1 (3.7-12.0)
PFI/TFI		
1-3 months	41	9.8 (2.7-23.1)
3-6 months	156	9.0 (5.1-14.6)
6-12 months	143	9.1 (4.9-15.0)
≥12 months	36	2.8 (0.1-14.5)
Platinum Sensitivity		
Platinum refractory	5	0.0 (0.0-52.2)
Platinum resistant-recurrent	140	8.6 (4.5-14.5)
Partial platinum-sensitive recurrent	128	8.6 (4.4-14.9)
Platinum-sensitive recurrent	18	5.6 (0.1-27.3)
Other	85	9.4 (4.2-17.7)
PD-L1 Status		
CPS ≥10	65	13.8 (6.5-24.7)
≥1 CPS <10	85	3.5 (0.7-10.0)
CPS <1	124	7.3 (3.4-13.3)
Unknown	102	10.8 (5.5-18.5)
Histology		
High grade serous	283	8.8 (5.8-12.8)
Endometrioid carcinoma	28	0.0 (0.0-12.3)
Clear cell carcinoma	19	21.1 (6.1-45.6)
Other	46	6.5 (1.4-17.9)

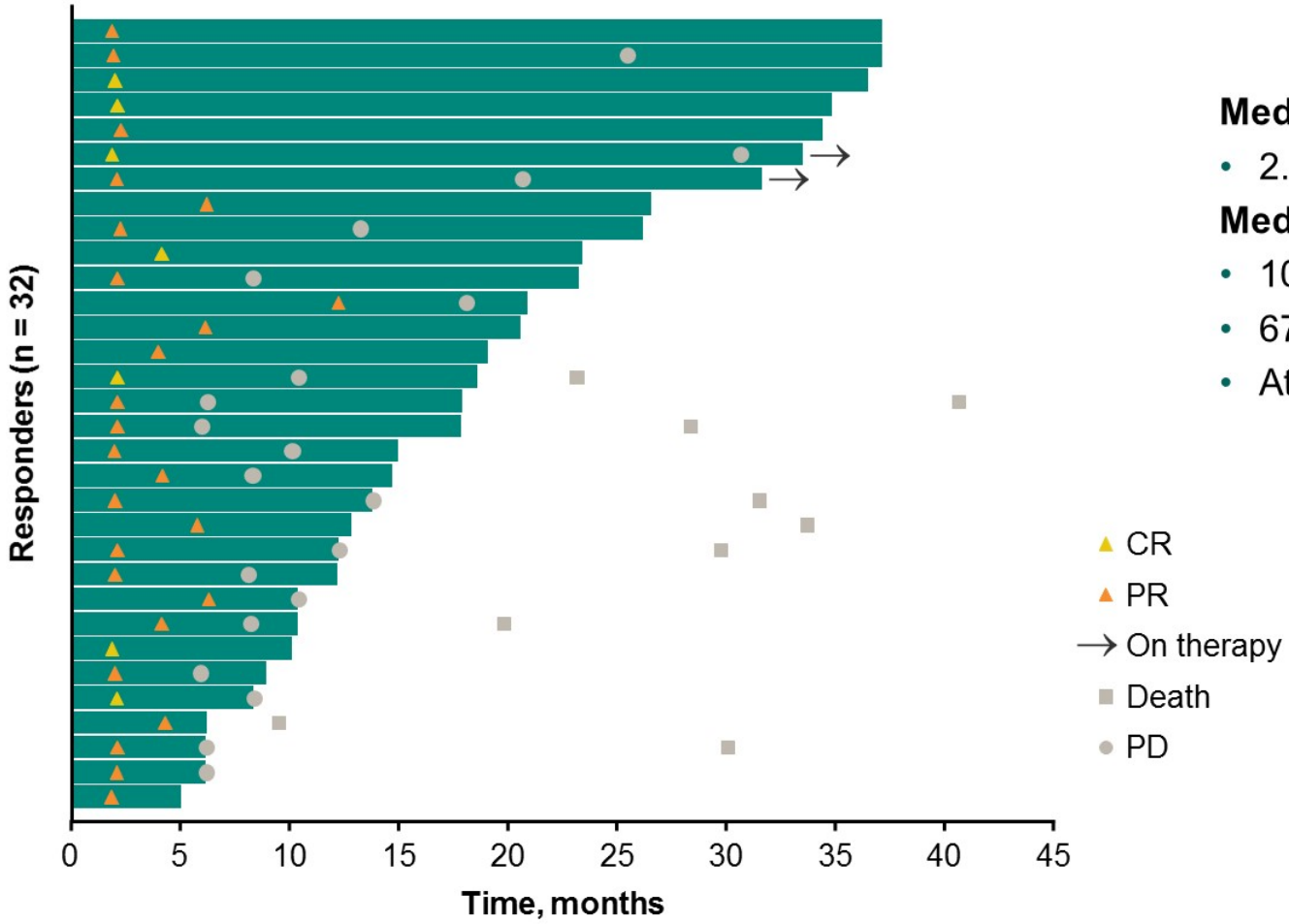


Platinum sensitivity only applies to subjects with platinum therapy in the last prior line of therapy. Based on RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1 per BICR, Blinded Independent Central Review. All Subjects as Treated Population. Database cut-off date: September 18, 2019.

Courtesy of Robert L Coleman, MD

Matulonis UA et al. ASCO 2020;Abstract 6005.

KEYNOTE-100: Treatment Exposure and Duration of Response in Cohorts A + B — Based on RECIST v1.1 per BICR



Median time to response[a]

- 2.1 months (range, 1.8 - 12.3 months)

Median duration of response[a]

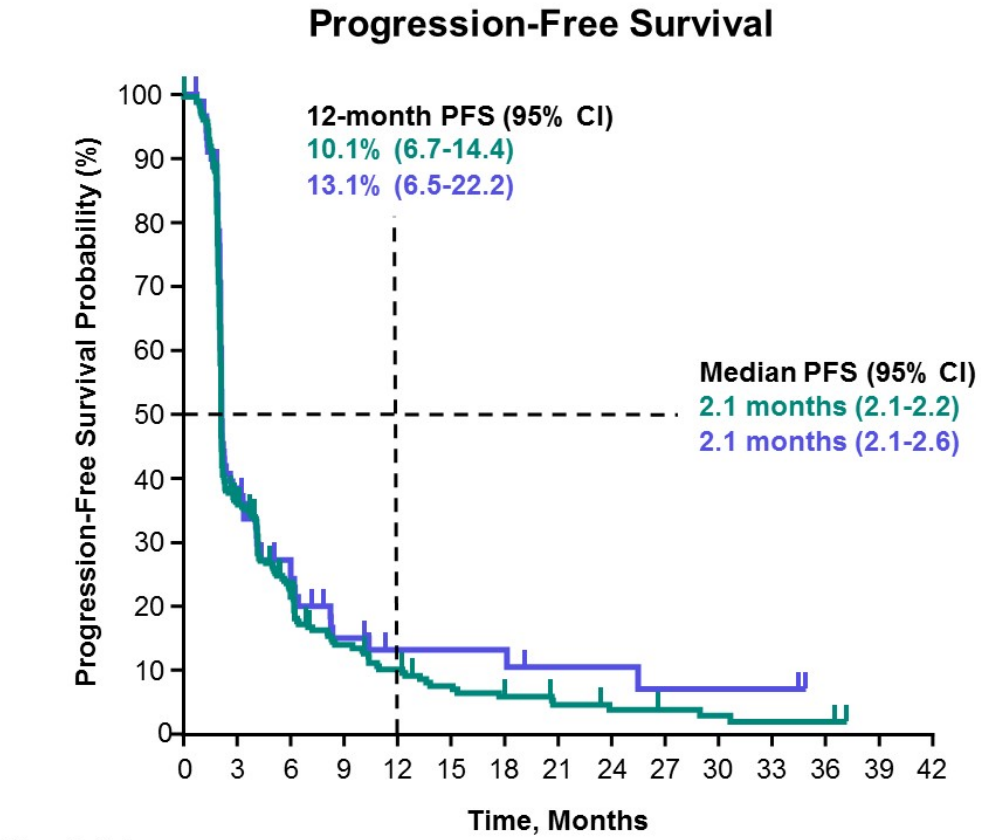
- 10.2 months (range, 3.3+ - 35.4+ months)[b]
- 67.7% of responses lasted ≥6 months[b]
- At data cut-off, 4/32 responses were ongoing

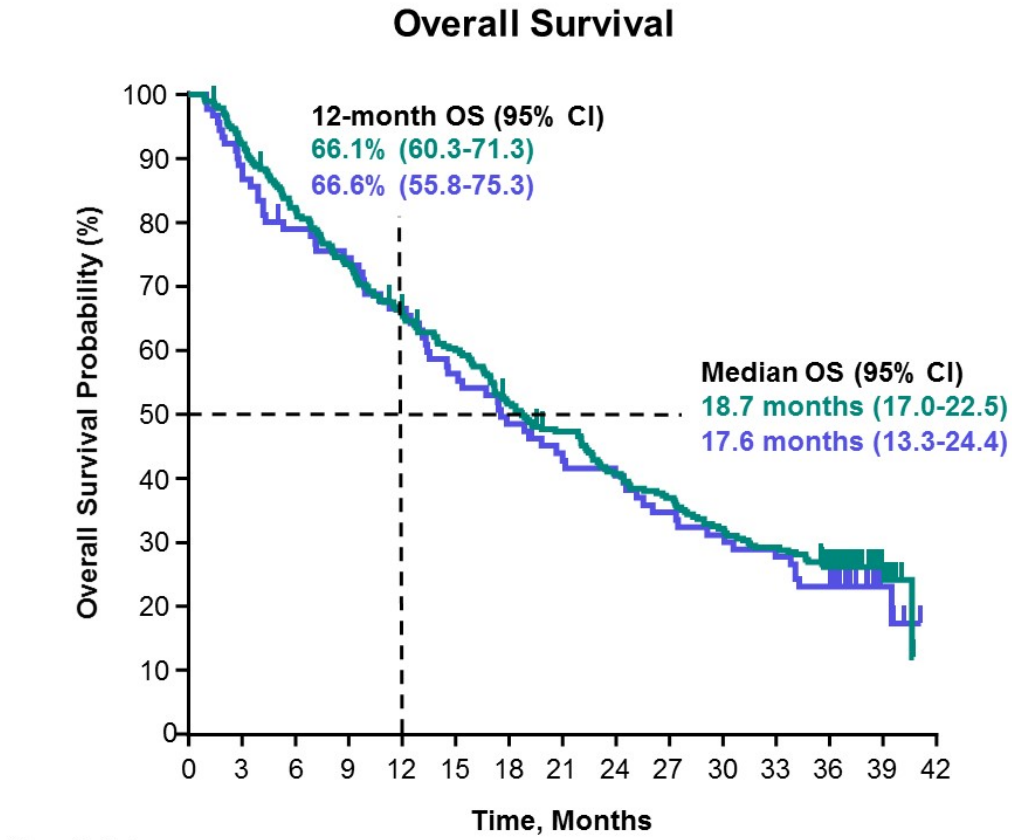
RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1. BICR, Blinded Independent Central Review. All Subjects as Treated Population. Median follow-up: 37.8 months (range, 35.9 - 42.0 months). [a]Includes patients with a confirmed PR or better per RECIST v1.1 by BICR (n = 32). [b]Kaplan-Meier estimate. Database cut-off date: September 18, 2019.

Courtesy of Robert L Coleman, MD

Matulonis UA et al. ASCO 2020;Abstract 6005.

KEYNOTE-100: Progression-Free Survival and Overall Survival





Progression-free survival based on RECIST v1.1 per BICR. RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1. BICR, Blinded Independent Central Review.
All Subjects as Treated Population. Database cut-off date: September 18, 2019.

Courtesy of Robert L Coleman, MD

Matulonis UA et al. ASCO 2020;Abstract 6005.

KEYNOTE-100: Efficacy by PD-L1 Expression — Cohort A Confirmed Response Rates Based on RECIST v1.1 per BICR

	Cohort A Training Set N = 97			Cohort A Validation Set N = 188			All Cohort A N = 285		
	CPS <1 n = 34	**CPS ≥1 n = 59**	**CPS ≥10 n = 20**	**CPS <1 n = 73**	**CPS ≥1 n = 88**	**CPS ≥10 n = 40**	**CPS <1 n = 107**	**CPS ≥1 n = 147**	**CPS ≥10 n = 60**
ORR % (95% CI)	**2.9 (0.1 - 15.3)**	**16.9 (8.4 - 29.0)**	**30.0 (11.9 - 54.3)**	**4.1 (0.9 - 11.5)**	**5.7 (1.9 - 12.8)**	**10.0 (2.8 - 23.7)**	**3.7 (1.0 - 9.3)**	**10.2 (5.8 - 16.3)**	**16.7 (8.3 - 28.5)**
DCR % (95% CI)	29.4 (15.1 - 47.5)	39.0 (26.5 - 52.6)	50.0 (27.2 - 72.8)	31.5 (21.1 - 43.4)	37.5 (27.4-48.5)	35.0 (20.6-51.7)	30.8 (22.3-40.5)	38.1 (30.2 - 46.5)	40.0 (27.6 - 53.5)
Best overall response									
Complete response n (%)	0 (0.0)	3 (5.1)	3 (15.0)	0 (0.0)	2 (2.3)	2 (5.0)	0 (0.0)	5 (3.4)	5 (8.3)
Partial response n (%)	1 (2.9)	7 (11.9)	3 (15.0)	3 (4.1)	3 (3.4)	2 (5.0)	4 (3.7)	10 (6.8)	5 (8.3)
Stable disease n (%)	9 (26.5)	13 (22.0)	4 (20.0)	20 (27.4)	28 (31.8)	10 (25.0)	29 (27.1)	41 (27.9)	14 (23.3)
Progressive disease n (%)	23 (67.6)	35 (59.3)	10 (50.0)	46 (63.0)	49 (55.7)	22 (55.0)	69 (64.5)	84 (57.1)	32 (53.3)

Courtesy of Robert L Coleman, MD

Matulonis UA, et al. J Clin Oncol. 2018;36(15)5511.; Lederman JA, et al. Ann Oncol. 2018;29(8):vii728.; Matulonis UA, et al. SGO 2019; Abstract 26.; Matulonis UA, et al. Ann Oncol. 2019;30(7)L1080-1087.

KEYNOTE-100: Efficacy by PD-L1 Expression — Cohorts B and A + B
Confirmed Response Rates Based on RECIST v1.1 per BICR

	Cohort B N = 91			Cohorts A + B N = 376		
	CPS <1 n = 34	**CPS ≥1 n = 50**	**CPS ≥10 n = 22**	**CPS <1 n = 141**	**CPS ≥1 n = 197**	**CPS ≥10 n = 82**
ORR % (95% CI)	**8.8 (1.9 - 23.7)**	**10.0 (3.3 - 21.8)**	**18.2 (5.2 - 40.3)**	**5.0 (2.0 - 10.0)**	**10.2 (6.3 - 15.2)**	**17.1 (9.7 - 27.0)**
DCR % (95% CI)	38.2 (22.2 - 56.4)	38.0 (24.7 - 52.8)	45.5 (24.4 - 67.8)	32.6 (25.0 - 41.0)	38.1 (31.3 - 45.2)	41.5 (30.7 - 52.9)
Best overall response						
Complete response n (%)	0 (0.0)	2 (4.0)	2 (9.1)	0 (0.0)	7 (3.6)	7 (8.5)
Partial response n (%)	3 (8.8)	3 (6.0)	2 (9.1)	7 (5.0)	13 (6.6)	7 (8.5)
Stable disease n (%)	10 (29.4)	14 (28.0)	6 (27.3)	39 (27.7)	55 (27.9)	20 (24.4)
Progressive disease n (%)	18 (52.9)	29 (58.0)	12 (54.5)	87 (61.7)	113 (57.4)	44 (53.7)

Courtesy of Robert L Coleman, MD

Matulonis UA, et al. J Clin Oncol. 2018;36(15)5511.; Lederman JA, et al. Ann Oncol. 2018;29(8):vii728.; Matulonis UA, et al. SGO 2019; Abstract 26.; Matulonis UA, et al. Ann Oncol. 2019;30(7)L1080-1087.

KEYNOTE-100: BRCA Mutation Status and Best Overall Response

BRCA Status[b]	No Response n (%)	Response n (%)	*P*
***BRCA* wild-type**	55 (91.7%)	5 (8.3%)	0.65
***BRCA* mutation**	10 (90.9%)	1 (9.1%)	

- *BRCA* was not statistically significantly associated with best overall response

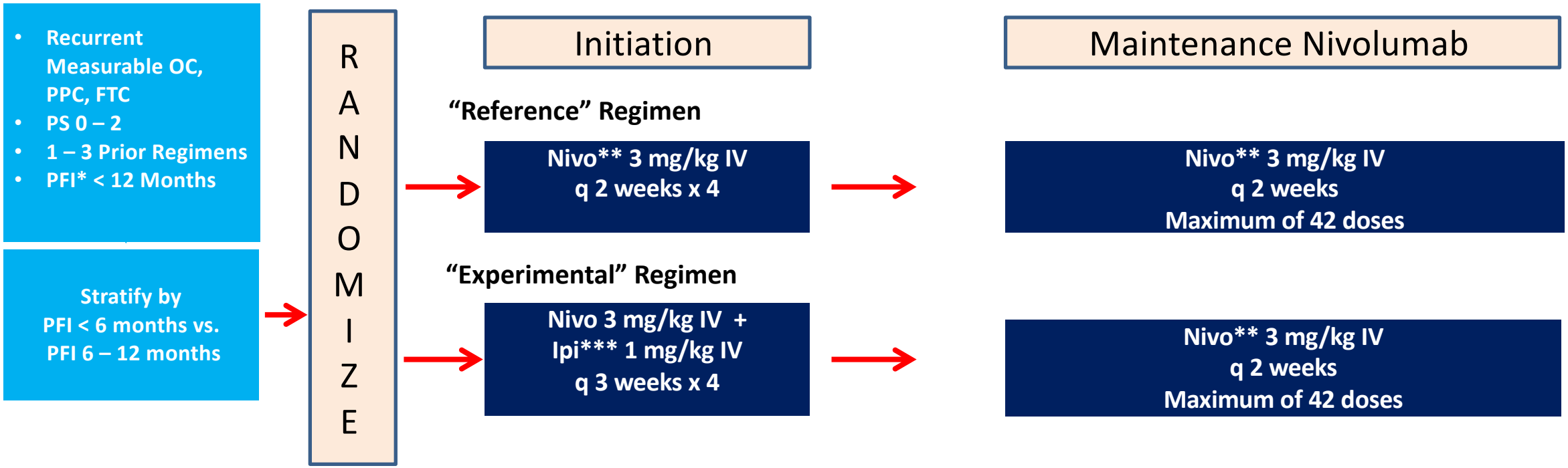
Courtesy of Robert L Coleman, MD

CONCLUSIONS

- In unrestricted populations of recurrent ovarian cancer response rate and PFS to single agent pembrolizumab is modest
- Duration of response is substantial in responding patients
- Cohorts A and B have similar outcomes
- No obvious interaction with BRCA status
- Biomarker CPS score may be helpful in identifying candidates for use

Courtesy of Robert L Coleman, MD

Final Preview of NRG GY003: Phase II Randomized Trial of Nivolumab with or without Ipilimumab in Patients with Persistent or Recurrent Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancer



Courtesy of Robert L Coleman, MD

Burger, IGCS, Kyoto, Japan 2018

GY003: Phase II (Ipi/nivo vs nivo)

- N = 100 patients
  - 49 pts Nivo “control”
  - 51 pts Ipi/Nivo
- Demographics
  - Median age: 62
  - HGSOC: 82%
- Response window 6 months
- Gr 3+ toxicity
  - 27 (55%) Nivolumab
  - 34 (67%) in combination
  - No Grade 5 events

Outcome	Nivo	Ipi + Nivo
Response	6/49 **(12%)**	16/51 **(31%)**
HR_{PFS}	0.53 (0.34-0.82)	
HR_{Death}	0.79 (0.44-1.42)	

Courtesy of Robert L Coleman, MD

Zamairin J Clin Oncol 2020

GY003: Phase II (Ipi/nivo vs nivo)

- N = 100 patients
  - 49 pts Nivo “control”
  - 51 pts Ipi/Nivo
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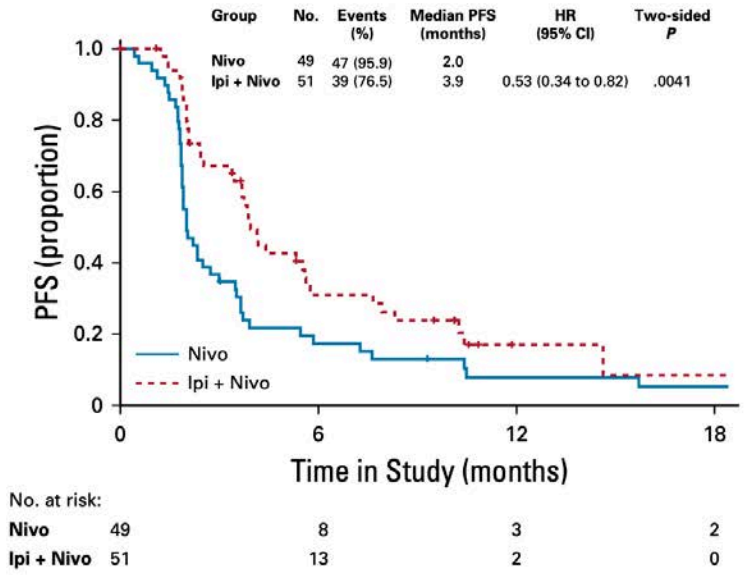

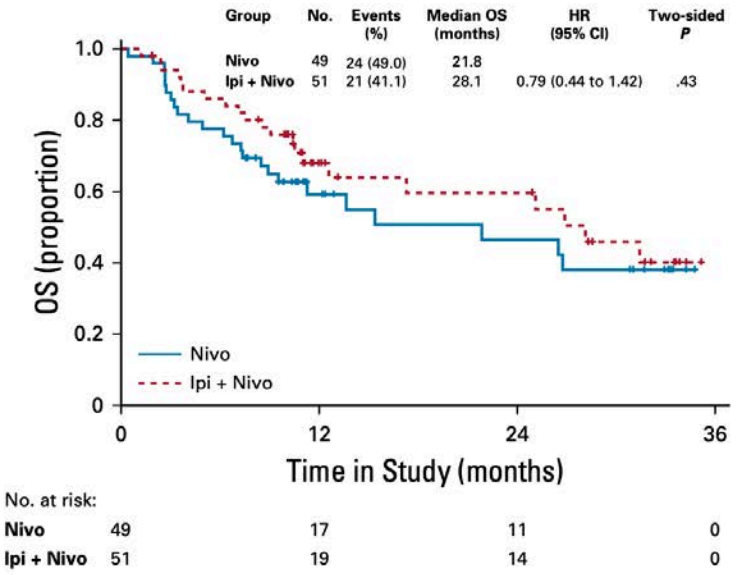

Courtesy of Robert L Coleman, MD

Zamairin J Clin Oncol 2020

CONCLUSIONS

- Single agent nivolumab has similar efficacy to other IO agents
- Similar to combination therapy in other disease sites, efficacy and toxicity appear to be enhanced with combination PD-1/L1 and CTLA-4
- Given efficacy characteristics, a defined site for use in recurrent patients is not established
- Current trials with combinations are ongoing in many settings of primary and recurrent ovarian cancer

Courtesy of Robert L Coleman, MD