Ovarian Cancer, Beyond Carboplatin and Paclitaxel

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Lecture outline

- Review historical perspective
- Review Sentinel trials
- Review recent developments
- Review treatment algorithms
- Questions

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Adjuvant chemotherapy after PDS (GOG 158)

Phase III Trial of Carboplatin and Paclitaxel Compared With Cisplatin and Paclitaxel in Patients With Optimally Resected Stage III Ovarian Cancer: A Gynecologic Oncology Group Study

Robert F. Ozols, Brian N. Bundy, Benjamin E. Greer, Jeffrey M. Fowler, Daniel Clarke-Pearson, Robert A. Burger…

Clin Oncol. 2003 Sep 1;21(17):3194-200

Adjuvant chemotherapy after PDS (GOG 158)

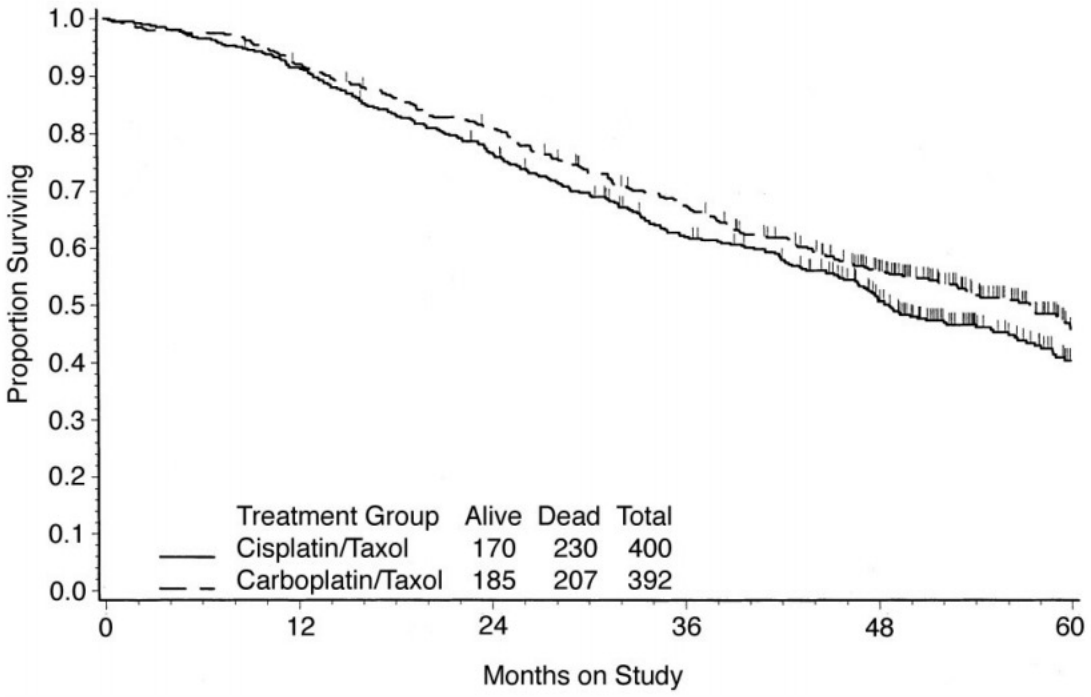

Fig 3. Observed survival by treatment group.

Clin Oncol. 2003 Sep 1;21(17):3194-200

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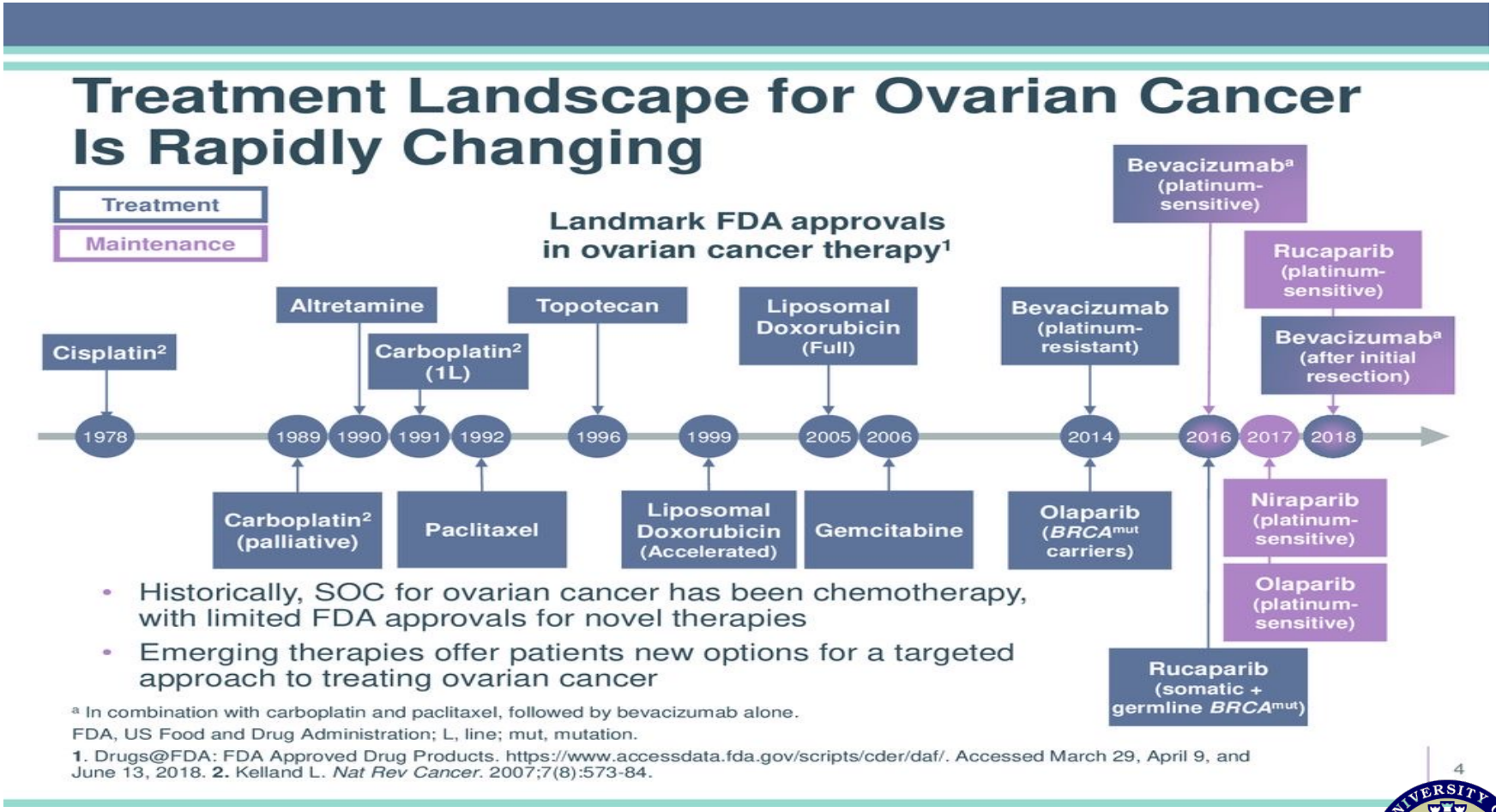
Ovarian cancer treatment landscape



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VEGF Inhibition

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Rationale for Targeting VEGF Pathway in the Treatment of Ovarian Cancer

- Human tumors
  - VEGF expression and degree of tumor angiogenesis (micro-vessel density) associated with
    - Ascites formation
    - Malignant progression
    - Poor prognosis

Yoneda et al, 1998; Ferrara, 1999; Dvorak, 2002; Gasparini et al, 1996; Hollingsworth et al, 1995; al, 1997; Alvarez et al, 1999.

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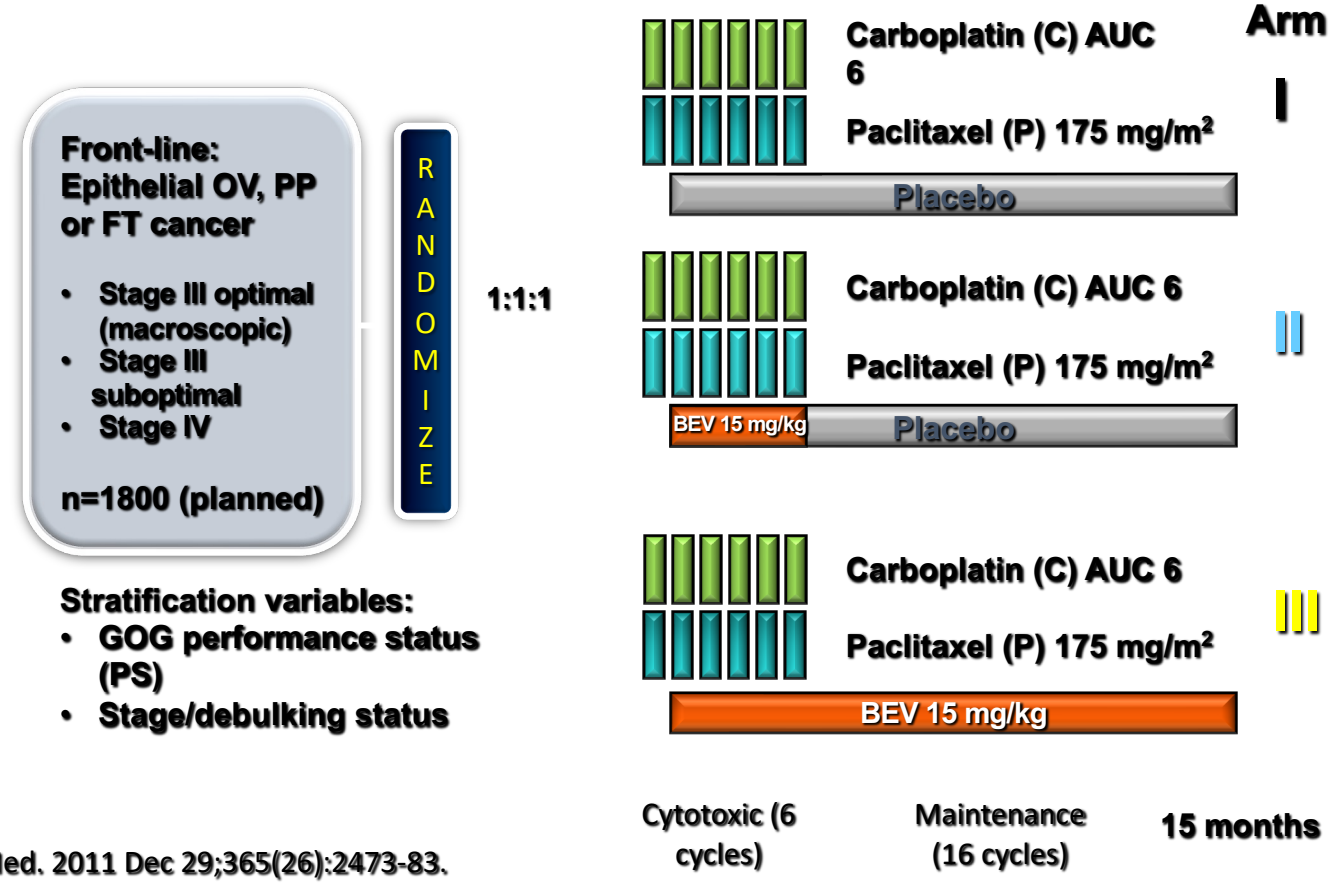
Bevacizumab (GOG 218)

Targeted therapy for ovarian, Bevacizumab



Burger, NEngl J Med. 2011 Dec 29;365(26):2473-83.

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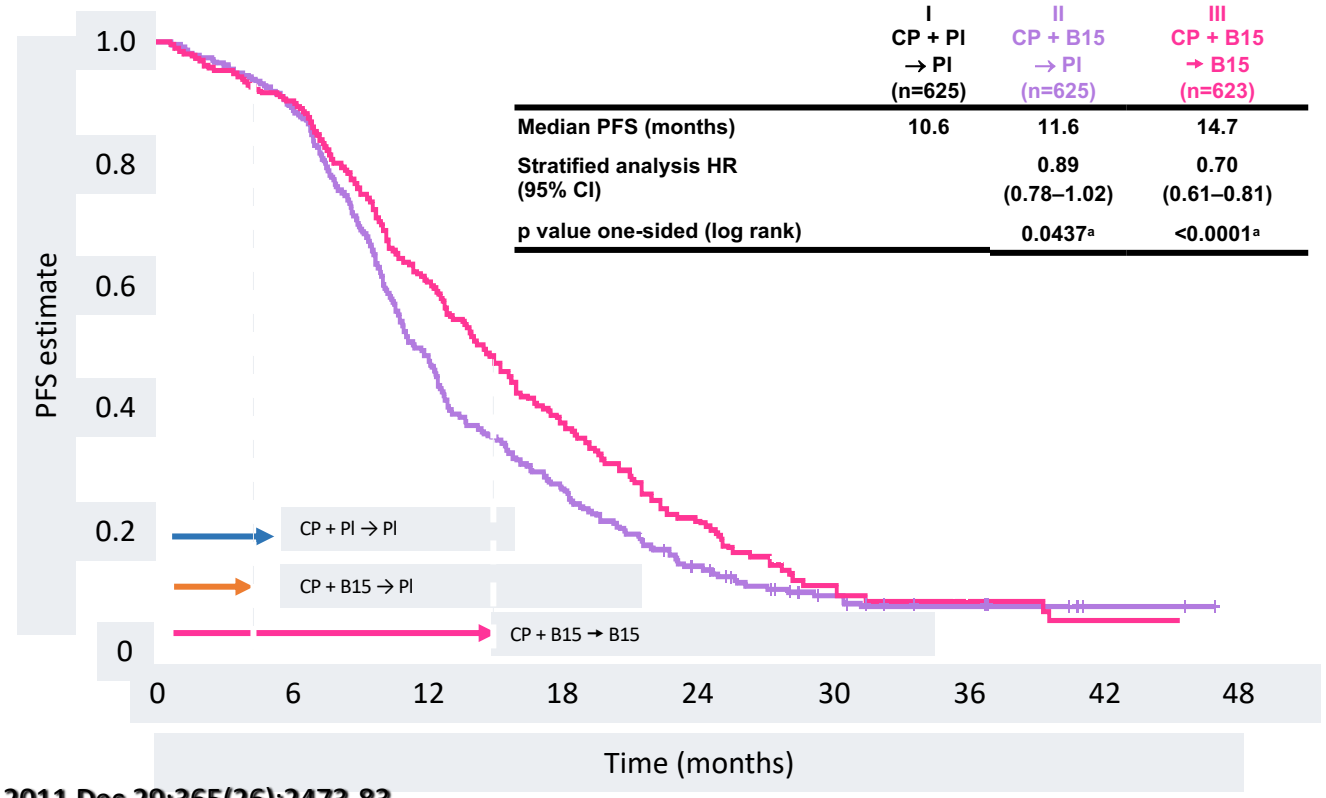
Targeted therapy for ovarian, Bevacizumab



	I CP + PI → PI (n=625)	II CP + B15 → PI (n=625)	III CP + B15 → B15 (n=623)
Median PFS (months)	10.6	11.6	14.7
Stratified analysis HR (95% CI)		0.89 (0.78–1.02)	0.70 (0.61–0.81)
p value one-sided (log rank)		0.0437[a]	<0.0001[a]

Burger, NEngl J Med. 2011 Dec 29;365(26):2473-83.

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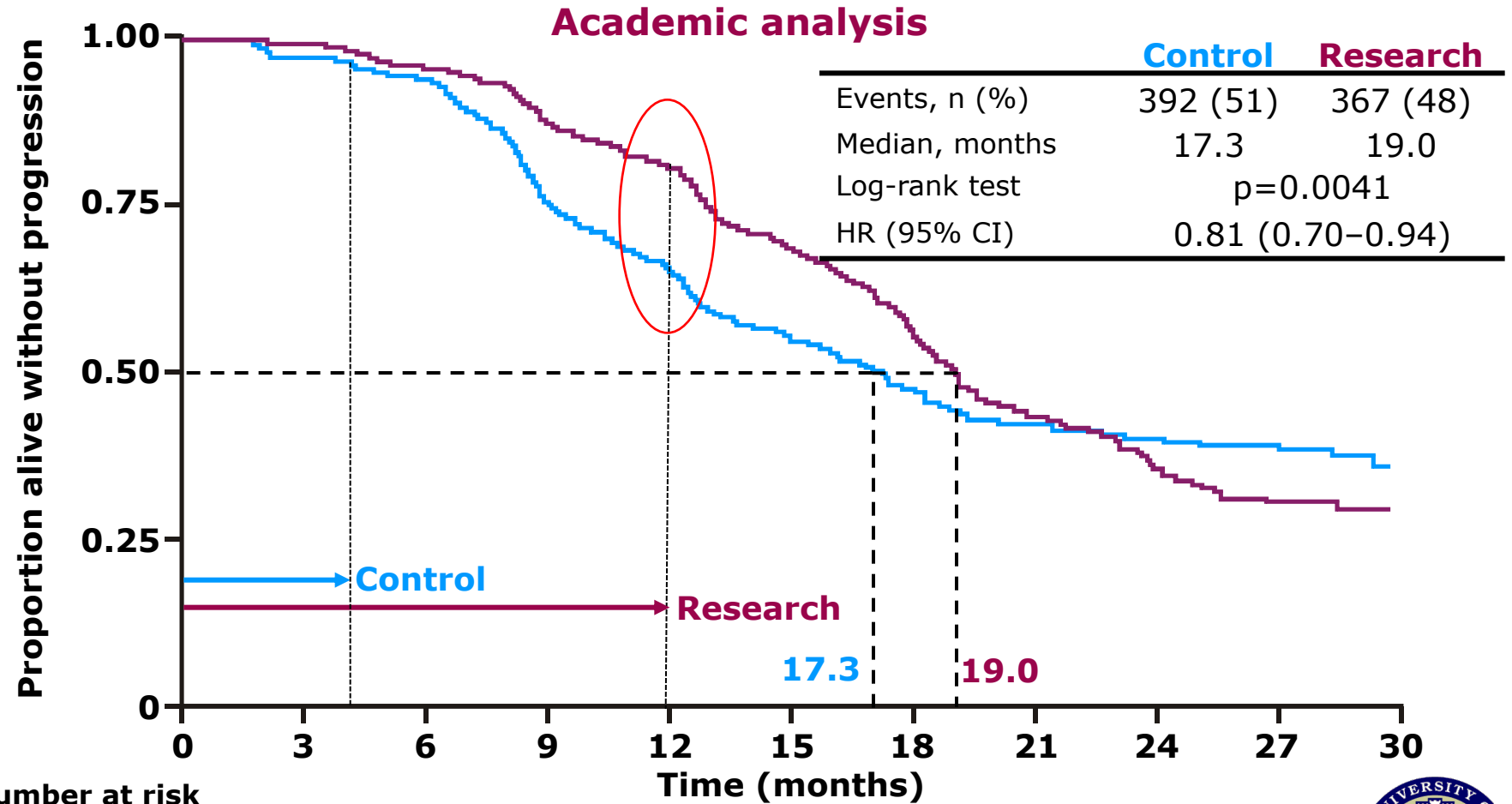
ICON7
Progression-free survival



Perren T, et al. NEJM 2011;365:2484

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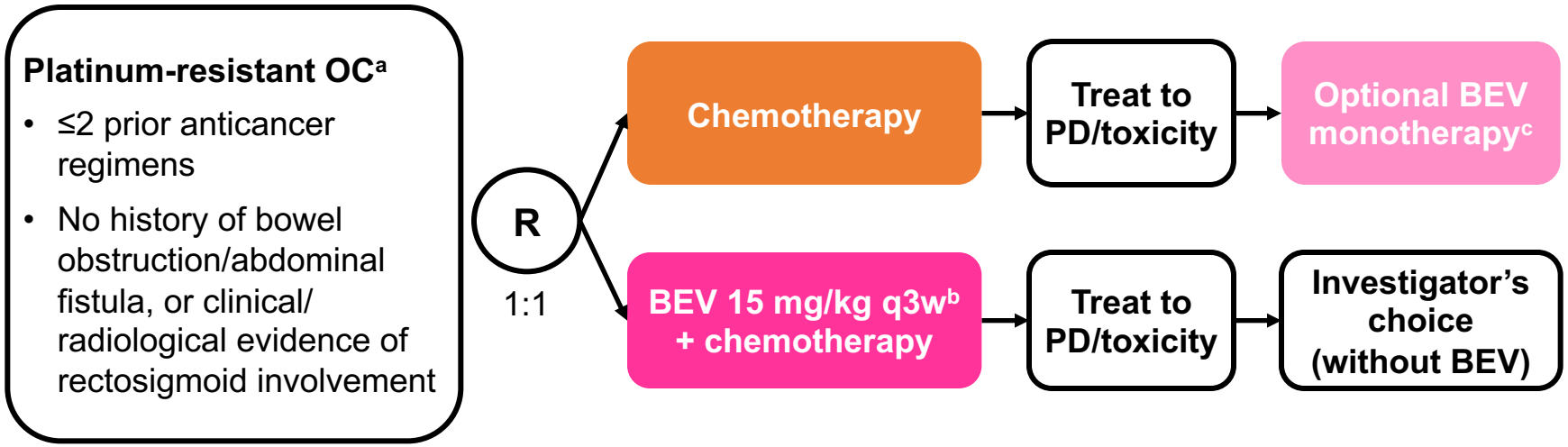
Recurrent disease

- Recurrence occurs in 75-80% of patients
- Platinum resistance/refractory disease in 10-15%
- Disease considered incurable at recurrence
- There multiple evolving

AURELIA trial design



Stratification factors:

- Chemotherapy selected
- Prior anti-angiogenic therapy
- Treatment-free interval (<3 vs 3–6 months from previous platinum to subsequent PD)

Chemotherapy options (investigator's choice):

- Paclitaxel 80 mg/m^2 days 1, 8, 15, & 22 q4w
- Topotecan 4 mg/m^2 days 1, 8, & 15 q4w (or 1.25 mg/m^2, days 1–5 q3w)
- PLD 40 mg/m^2 day 1 q4w

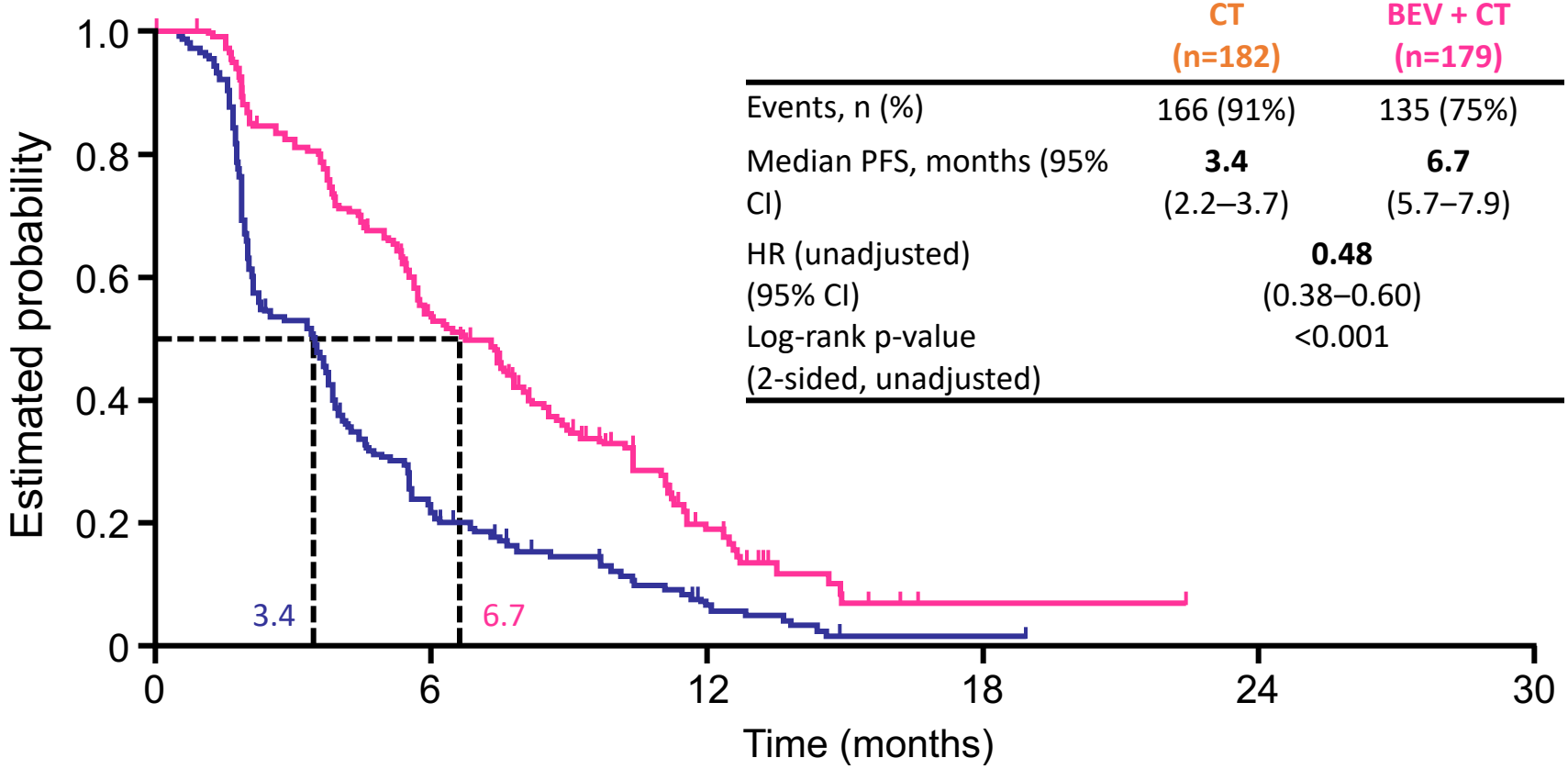
Pujade-Lauraine E. et al. J Clin Oncol 2014;32:[illegible]

PD = progressive disease

[a]Epithelial ovarian, primary peritoneal, or fallopian tube cancer; [b]Or 10 mg/kg q2w;

[c]15 mg/kg q3w, permitted on clear evidence of progression

AURELIA - Progression-free survival



	CT (n=182)	BEV + CT (n=179)
Events, n (%)	166 (91%)	135 (75%)
Median PFS, months (95% CI)	**3.4** (2.2–3.7)	**6.7** (5.7–7.9)
HR (unadjusted) (95% CI)	**0.48** (0.38–0.60)	
Log-rank p-value (2-sided, unadjusted)	<0.001	

No. at risk:

CT	182	93	37	20	8	1	1	0	0
BEV + CT	179	140	88	49	18	4	1	1	0

Median duration of follow-up: 13.9 months (CT arm) vs 13.0 months (BEV + CT arm)

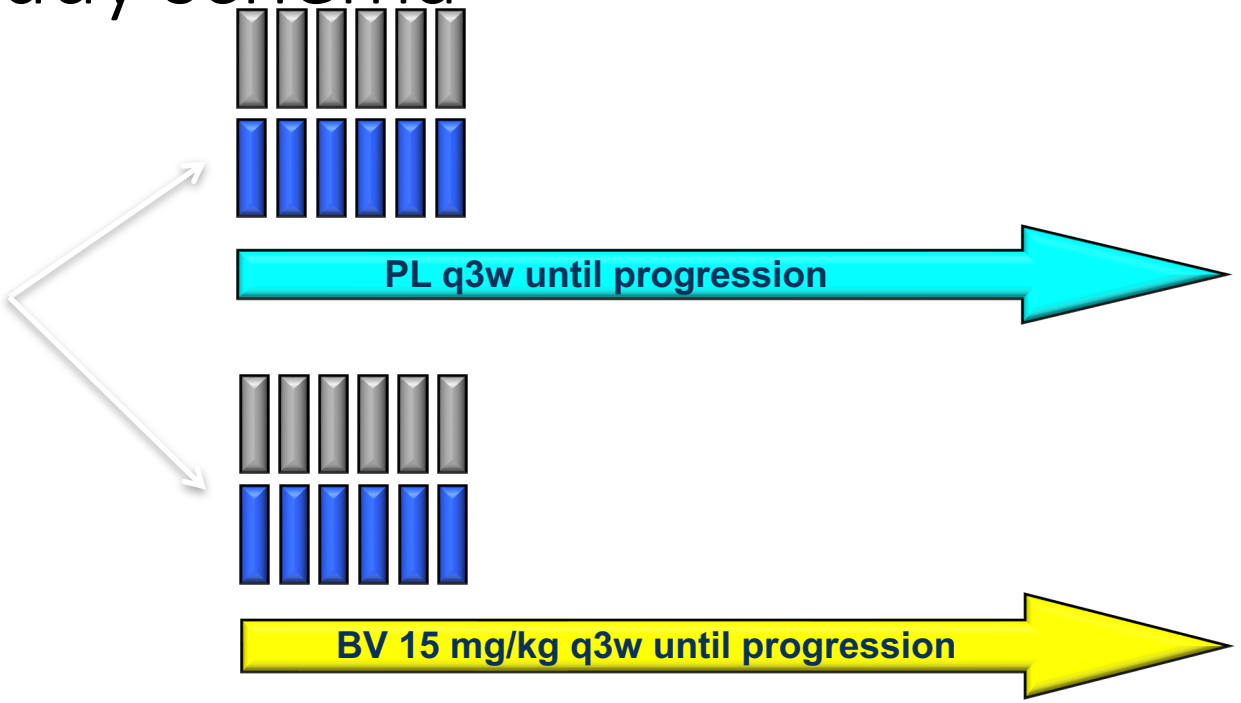
Pujade-Lauraine E. et al. LBA5002, ASCO 2012

OCEANS: Study schema

Platinum-sensitive recurrent OC[a]

- **Measurable disease**
- **ECOG 0/1**
- **No prior chemo for recurrent OC**
- **No prior BV**

(n=484)



months

Aghajanian C et al. J Clin Oncol 2012;30:2039

BV = bevacizumab; PL = placebo

[a]Epithelial ovarian, primary peritoneal, or fallopian tube cancer

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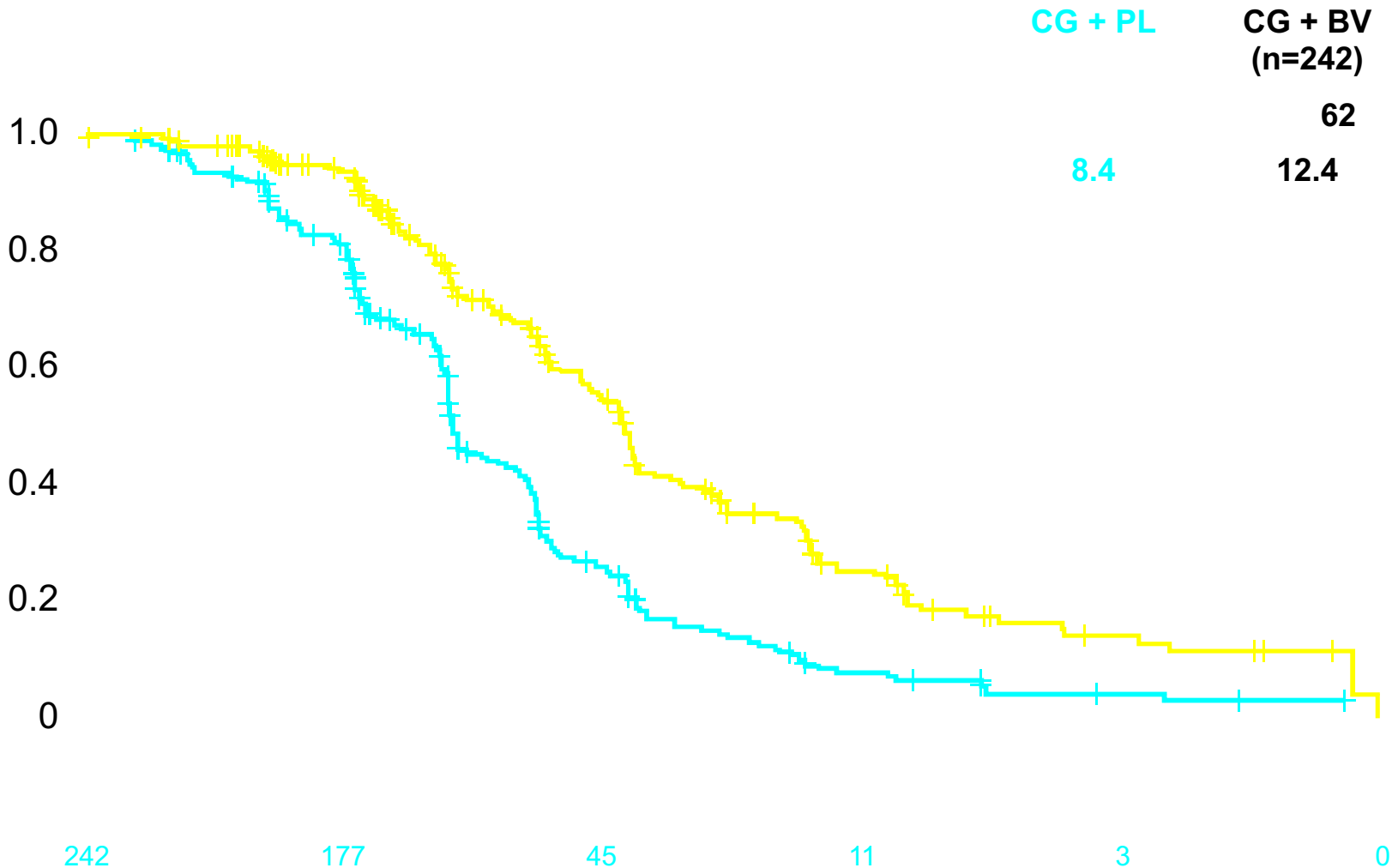
OCEANS: Primary analysis of PFS



Aghajanian C et al. J Clin Oncol. 2012; Apr 23 [Epub ahead of print]

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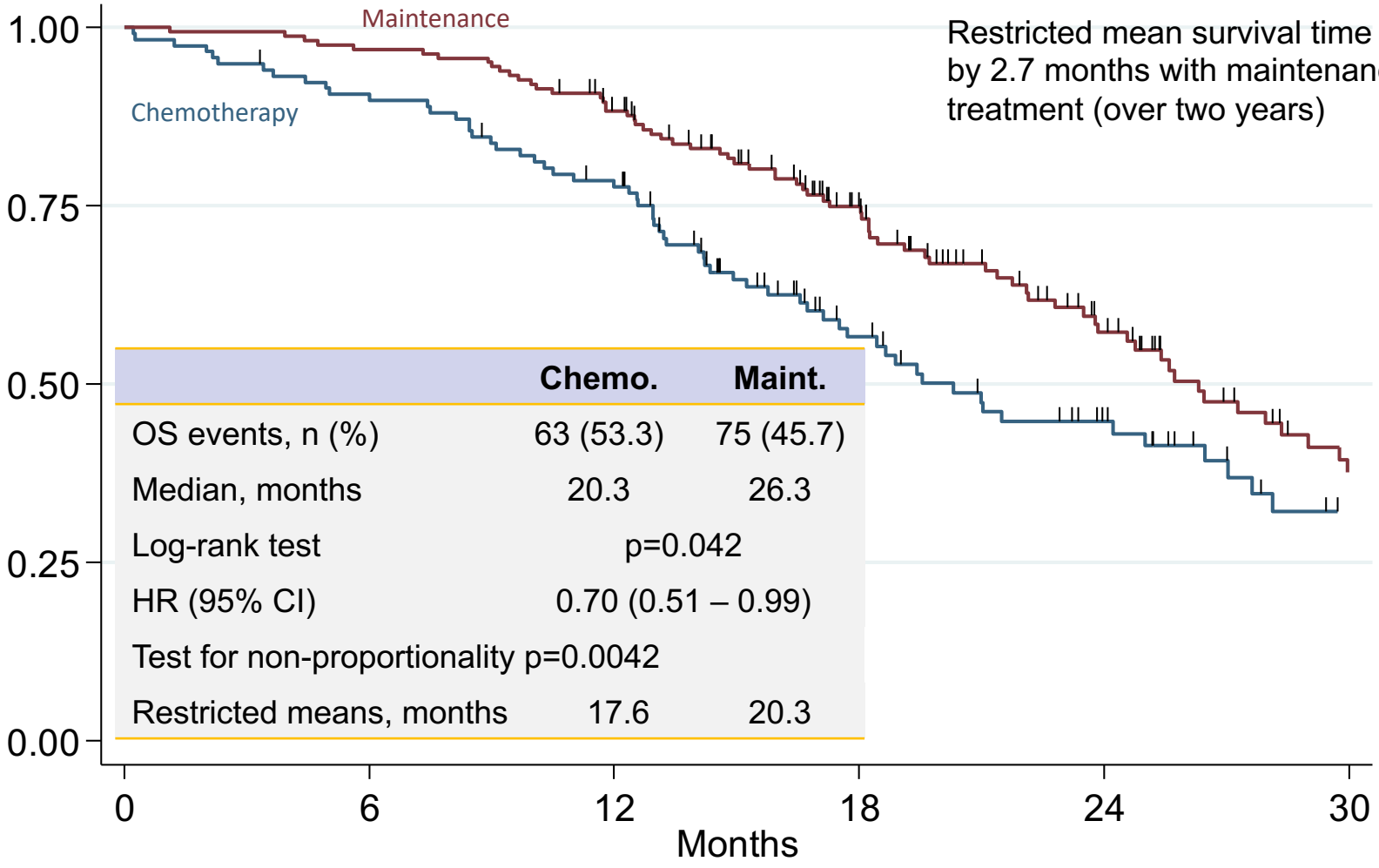
Overall survival



Restricted mean survival time increases by 2.7 months with maintenance treatment (over two years)

	Chemo.	Maint.
OS events, n (%)	63 (53.3)	75 (45.7)
Median, months	20.3	26.3
Log-rank test	p=0.042	
HR (95% CI)	0.70 (0.51 – 0.99)	
Test for non-proportionality	p=0.0042	
Restricted means, months	17.6	20.3

Chemo.	118	106	89	46	27	11
Maint.	164	159	139	89	48	22

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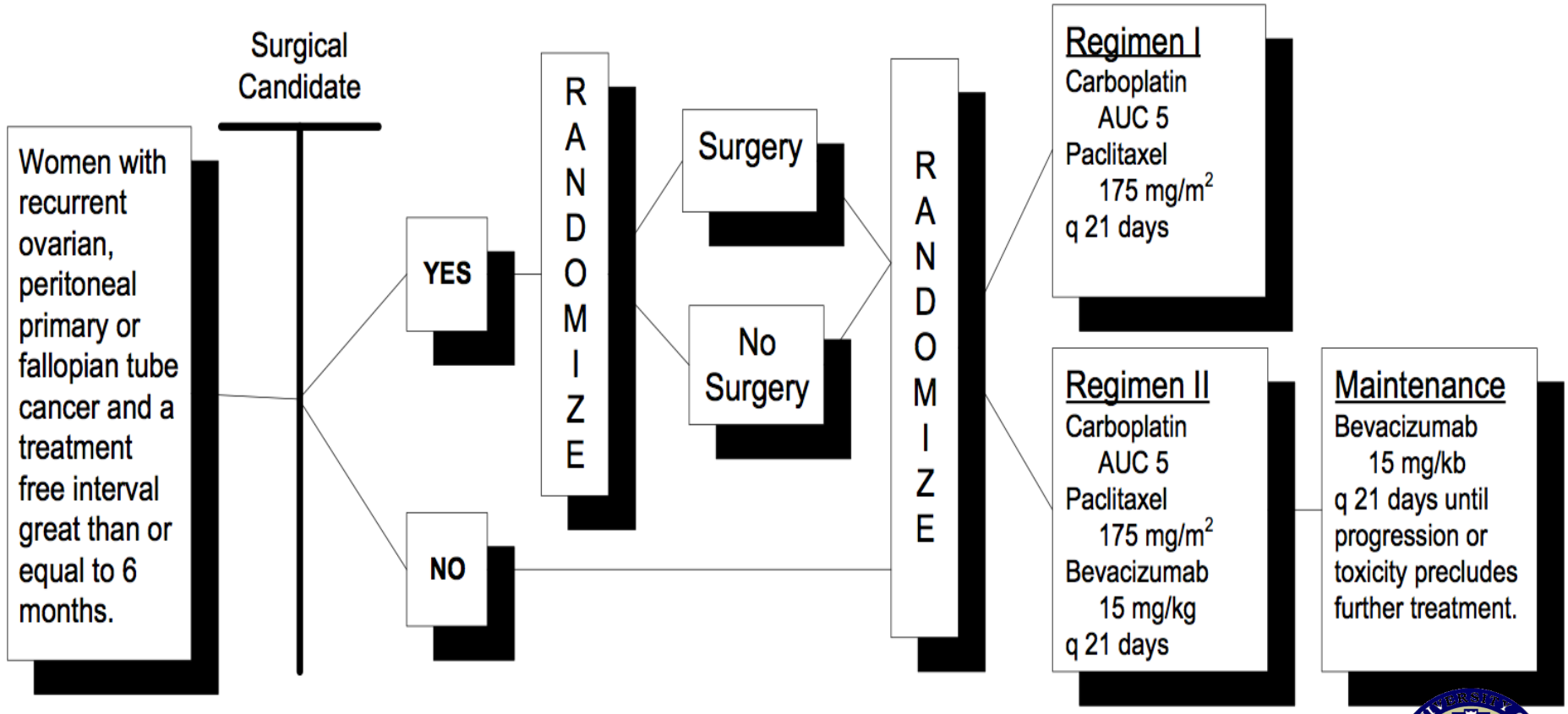
GOG 213: Schema



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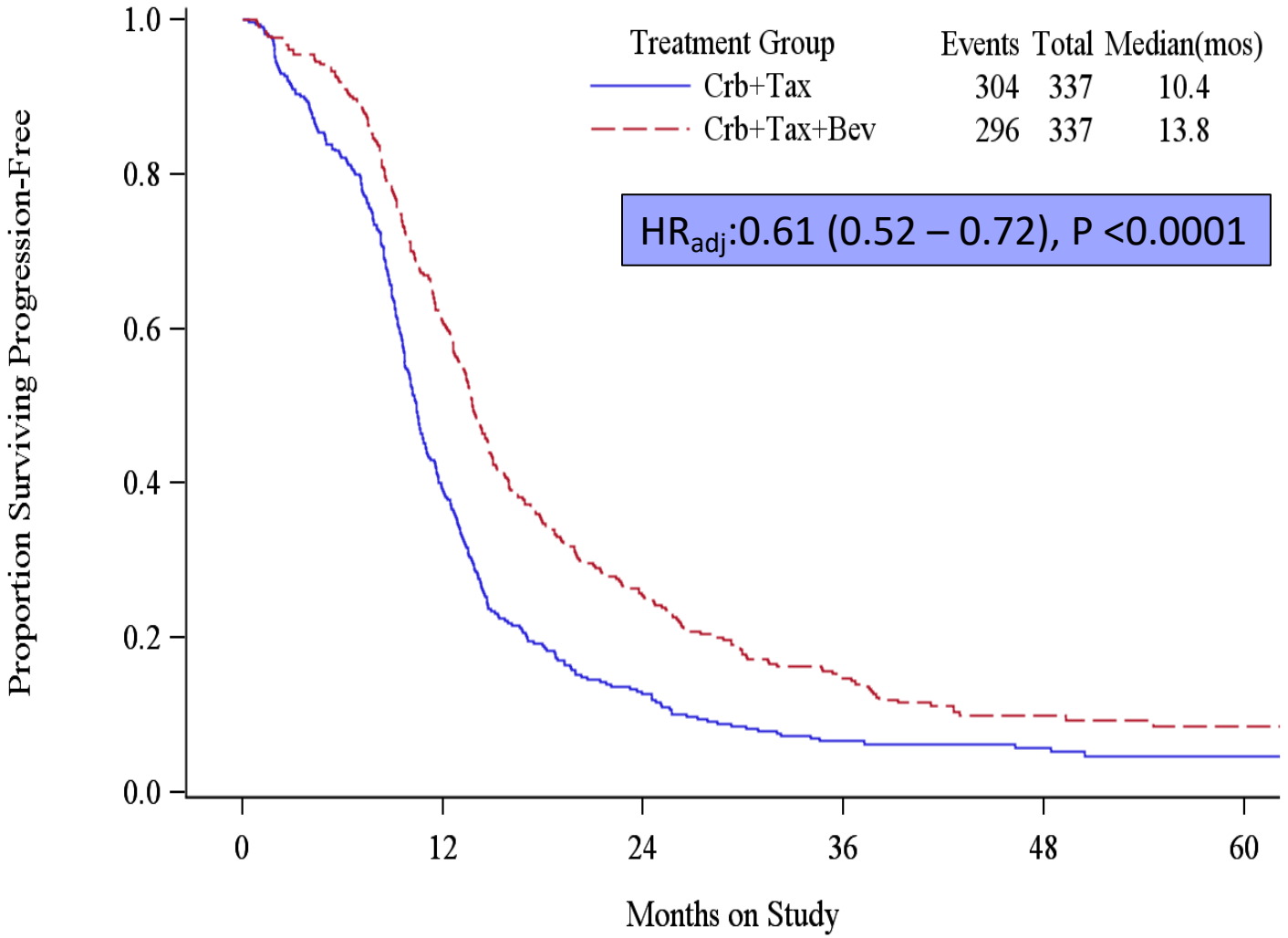
GOG 213 Treatment Outcome: PFS



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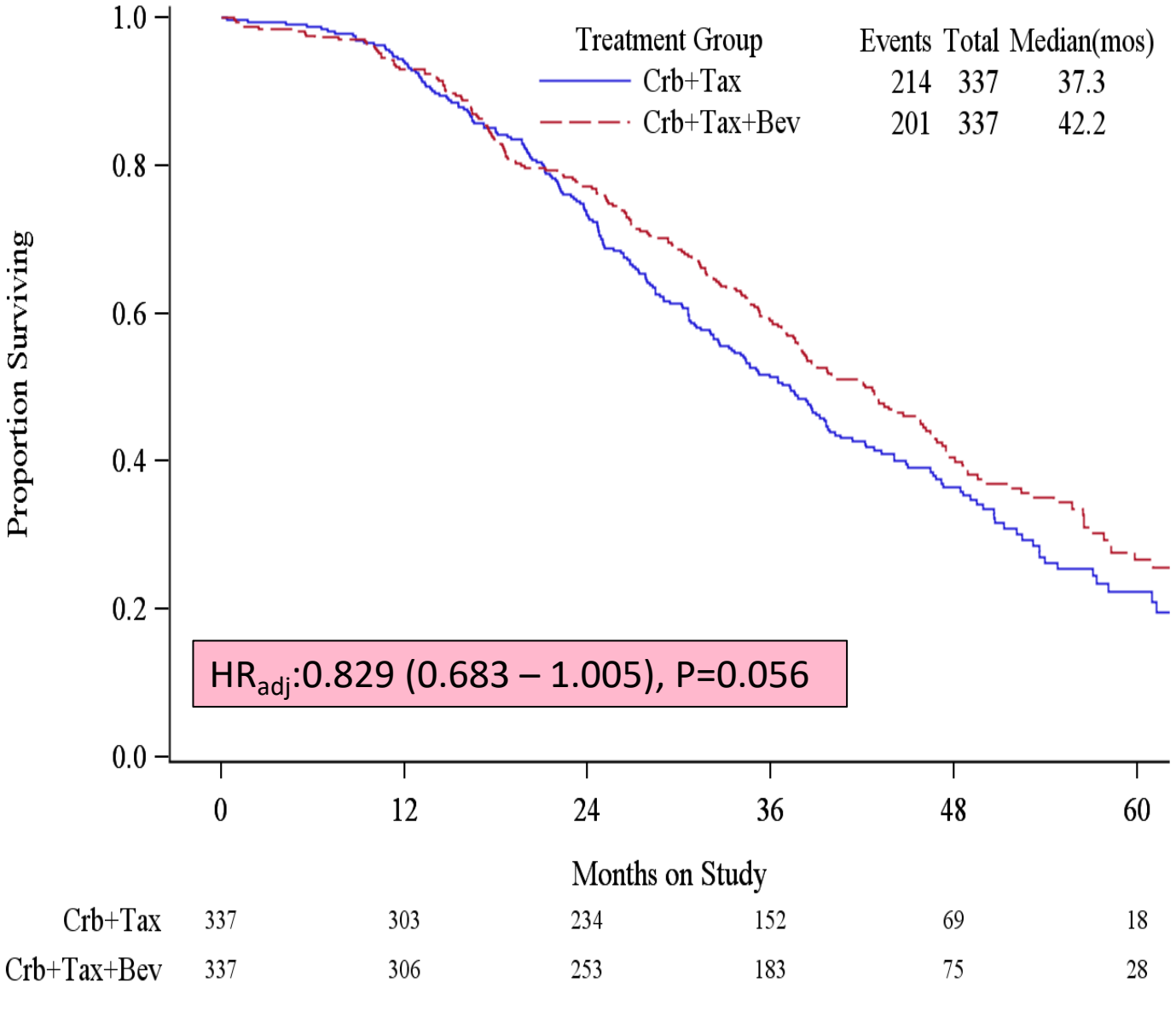
GOG 213 Treatment Outcome: OS



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PARP Inhibition

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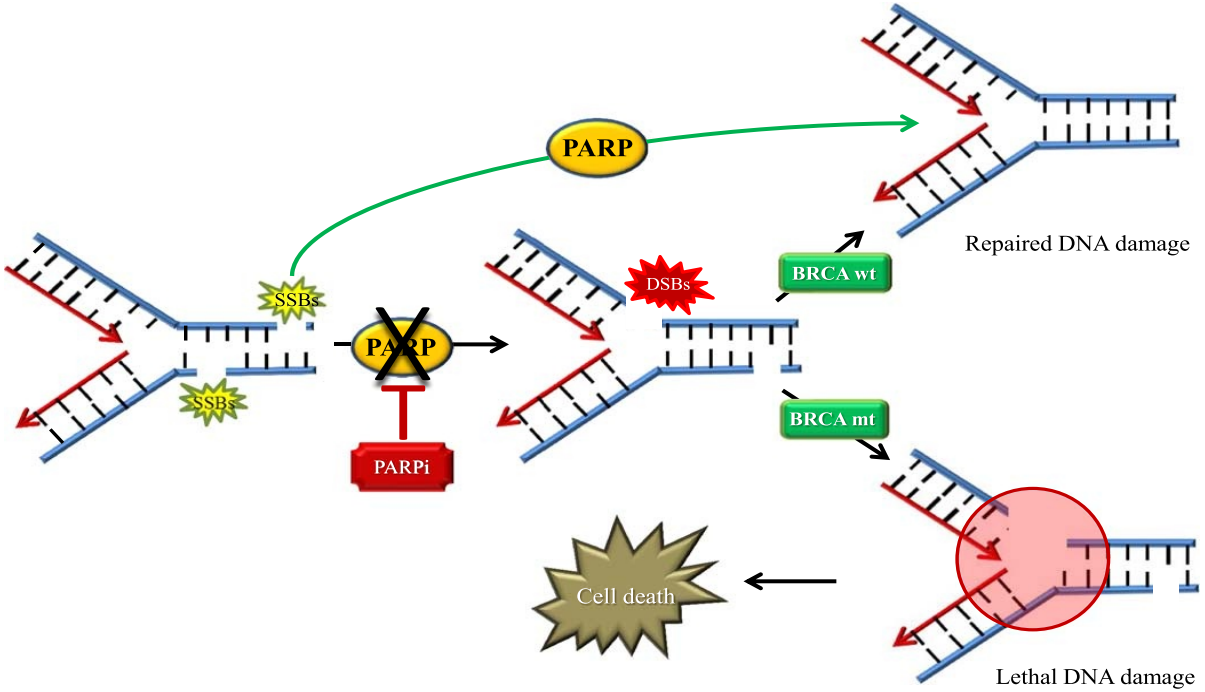
Homologous Recombination Repair



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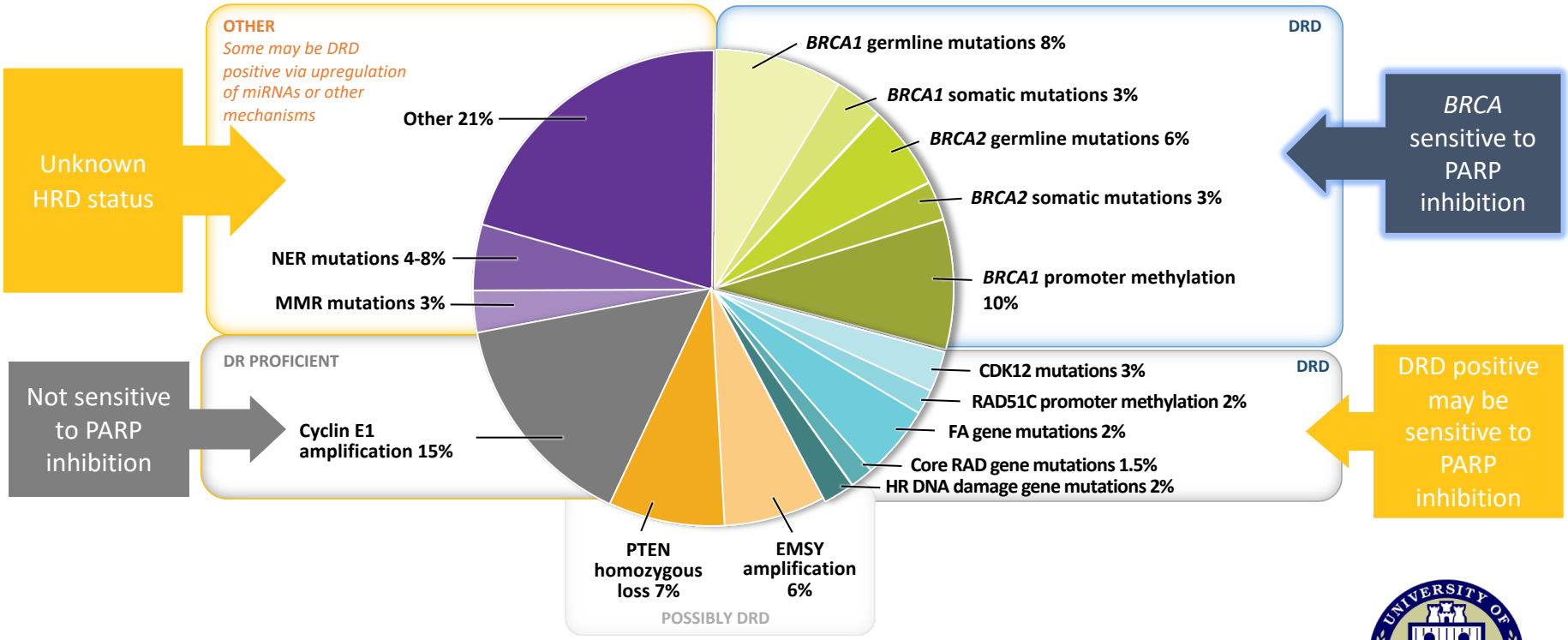
DNA-Repair Deficiency (DRD) Impacts at least 50% of Tumors

A subset of ovarian tumors may exhibit DRD in the absence of *BRCA1/2* mutations



CDK12, cyclin dependent kinase 12; EMSY, BRCA2-interacting transcriptional repressor; FA, Fanconi anemia; MMR, mismatch repair; miRNA, micro messenger ribonucleic acid; NER, nucleotide excision repair; PTEN, phosphatase and tensin homolog.

Konstantinopoulos PA, et al. *Cancer Discov*. 2015;5:1137-1154.

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PARP inhibitors maintenance in recurrent ovarian cancer

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NOVA: Niraparib Maintenance in Patients with Recurrent Ovarian Cancer

Phase III, multicenter, randomized, double-blind, placebo controlled study

- **Platinum-sensitive recurrent high grade serous ovarian cancer**
- **≥2 prior regimens of platinum-based chemotherapy**
- **Received at least 4 cycles platinum-based therapy and, following treatment, have an investigator-defined CR or PR with no observable residual disease of <2cm and CA-125 WNL or a decrease of >90% that was stable for at least 7 days**

N=553

Primary Endpoint: PFS by central, blinded review

Tested at 100 events to achieve p<0.05

- **HRDpos population**
- Tested at 100 events to achieve p<0.05
- If test was positive then:
- Test overall non-gBRCAmut cohort (p<0.05

Mirza, N Engl J Med 2016; 375:2154-2164

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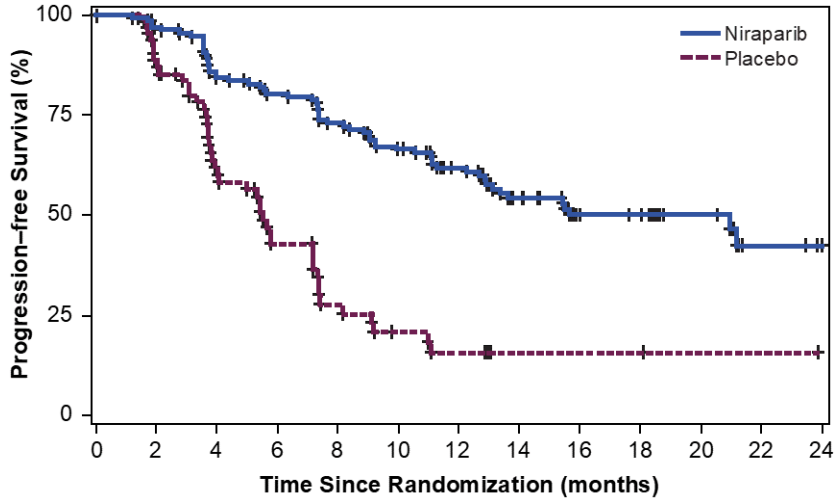
NOVA: gBRCAmut Progression-Free Survival



Treatment	PFS Median (95% CI) (Months)	Hazard Ratio (95% CI) p-value	% of Patients without Progression or Death	
			12 mo	18 mo
Niraparib (N=138)	21.0 (12.9, NR)	0.27 (0.173, 0.410) p<0.0001	62%	50%
Placebo (N=65)	5.5 (3.8, 7.2)		16%	16%

Mirza, N Engl J Med 2016; 375:2154-2164

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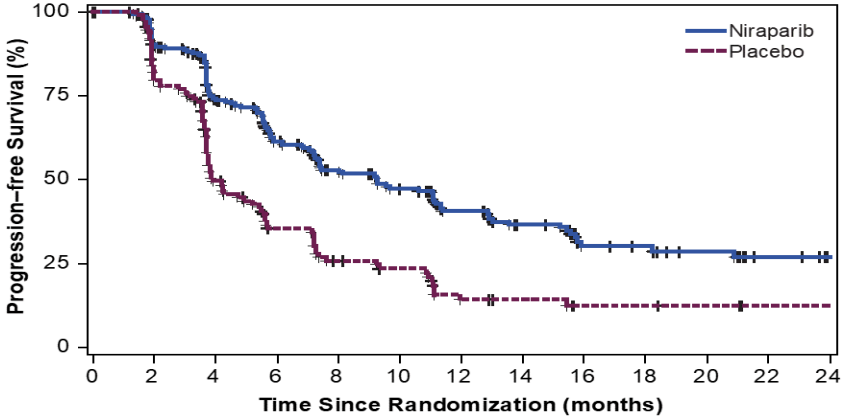
NOVA: Non-gBRCAmut Progression-Free Survival



Treatment	PFS Median (95% CI) (Months)	Hazard Ratio (95% CI) p-value	% of Patients without Progression or Death	
			12 mo	18 mo
Niraparib (N=234)	9.3 (7.2, 11.2)	0.45 (0.338, 0.607) p<0.0001	41%	30%
Placebo (N=116)	3.9 (3.7, 5.5)		14%	12%

Mirza, N Engl J Med 2016; 375:2154-2164

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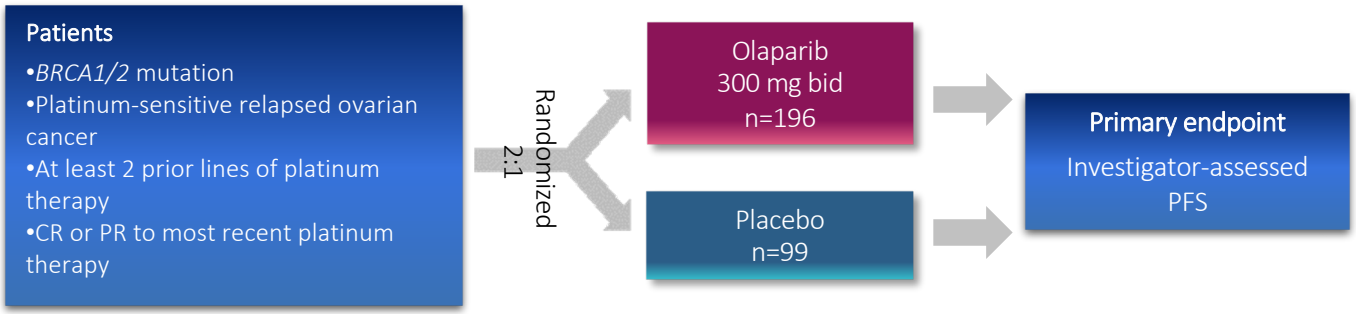
SOLO2/ENGOT-Ov21: Phase 3 Study Design



Sensitivity analysis: PFS by blinded independent central review (BICR)

- Key secondary endpoints:
  - Time to first subsequent therapy or death (TFST), time to second progression (PFS2), time to second subsequent therapy or death (TSST), overall survival (OS)
  - Safety, health-related quality of life (HRQoL*)

*Primary endpoint for HRQoL was trial outcome index (TOI) of the FACT-O (Functional Assessment of Cancer Therapy – Ovarian)

Pujade-Lauraine, Lancet Oncol. 2017 Sep;18(9):1274-1284.

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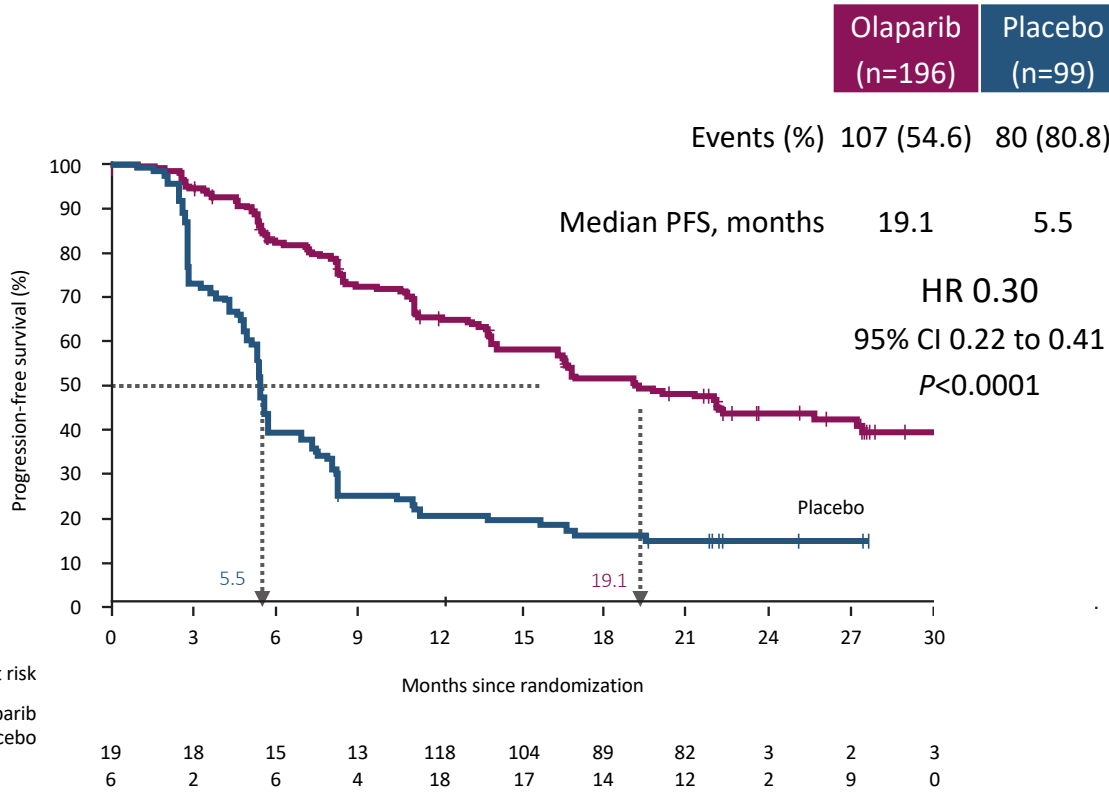
PFS by Investigator Assessment



Mirza, N Engl J Med 2016; 375:2154-2164

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STUDY 19

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Olaparib Maintenance Therapy in Platinum-Sensitive Relapsed Ovarian Cancer

Jonathan Lederman *et al.* N Engl J Med 2012; 366:1382-1392

University of Pittsburgh

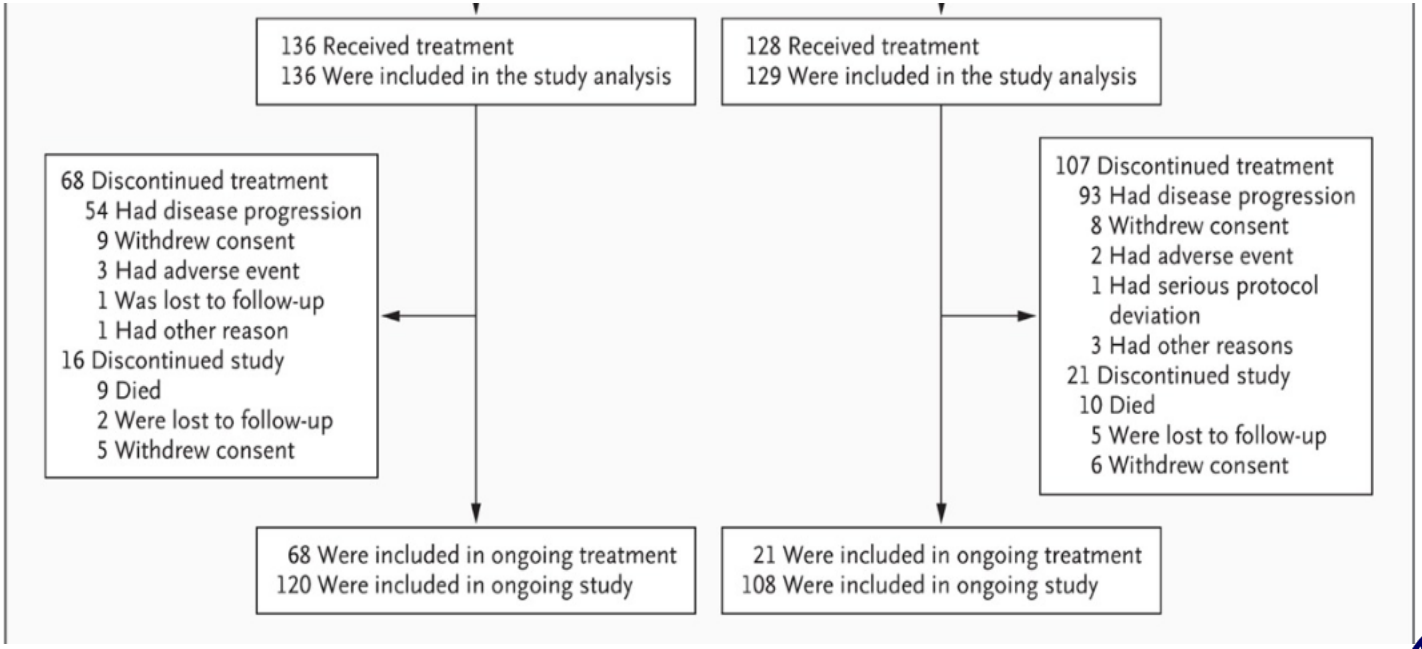
Study design

Randomized, double blind, placebo-controlled phase II study
Drug: Olaparib, 400mg PO twice/day

Jonathan, N Engl J Med 2012; 366:1382-1392

University of Pittsburgh

Randomization/enrollment



Jonathan, N Engl J Med 2012; 366:1382-1392

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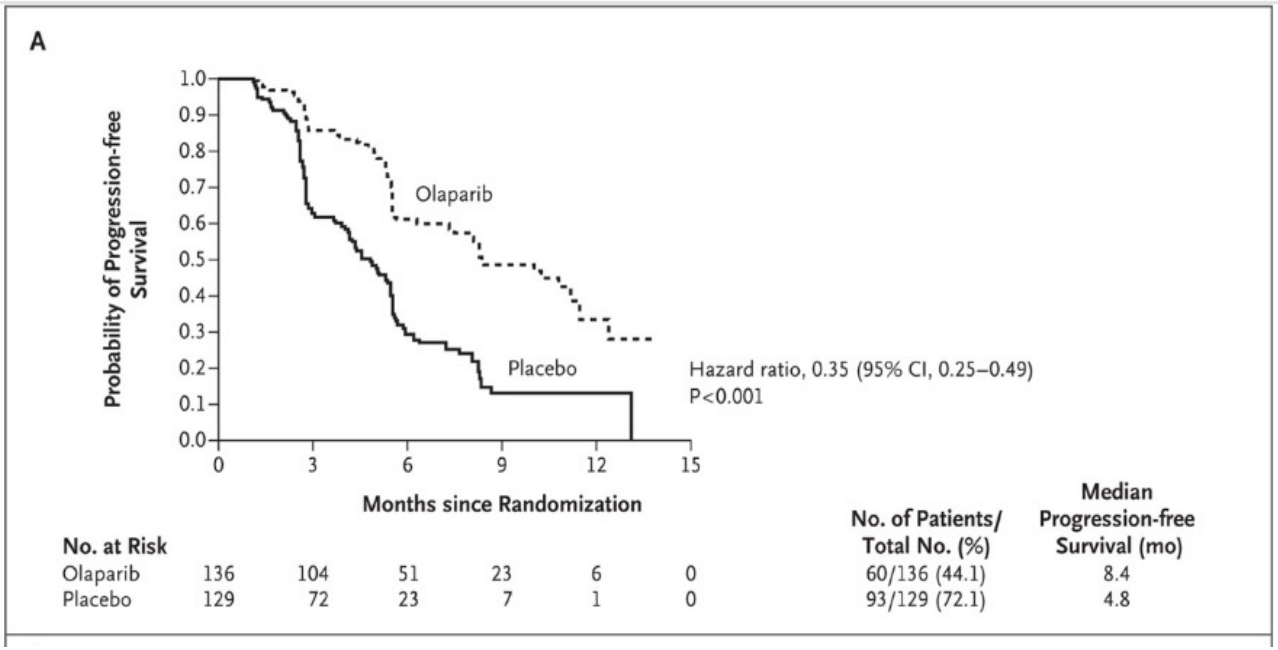
Result



Jonathan, N Engl J Med 2012; 366:1382-1392

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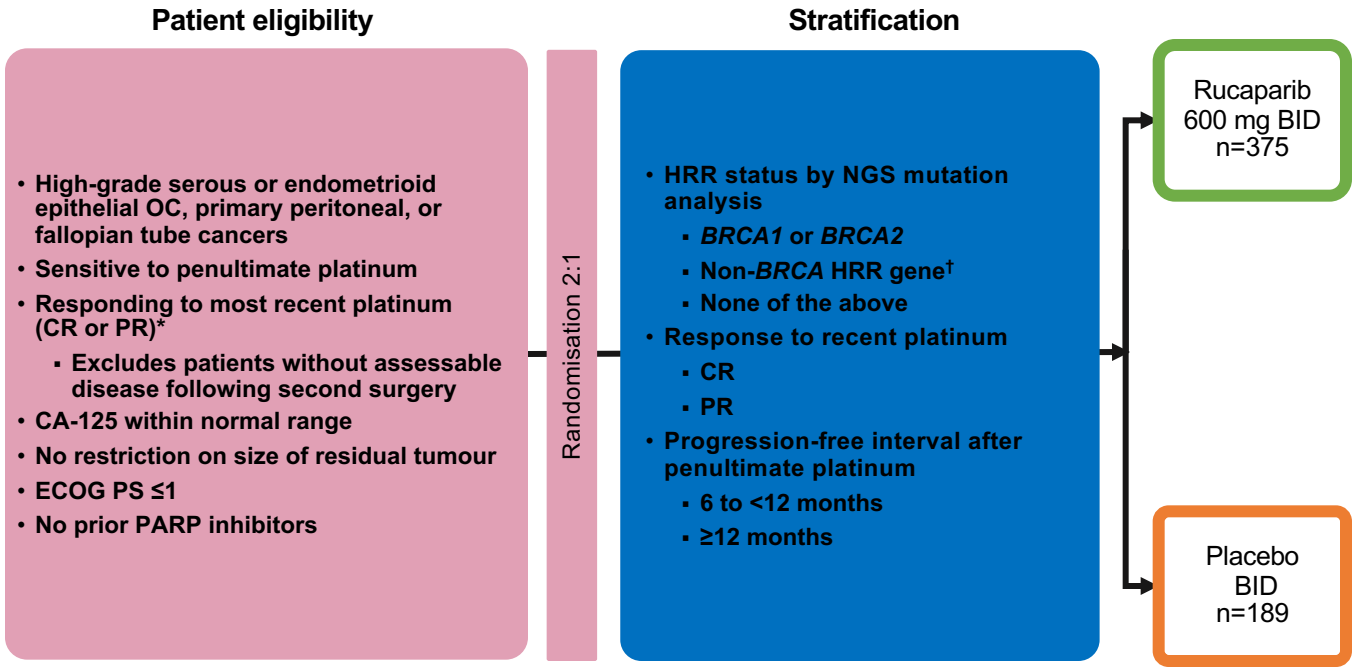
ARIEL3: Study Design



Lancet. 2017 Oct 28;390(10106):1949-1961

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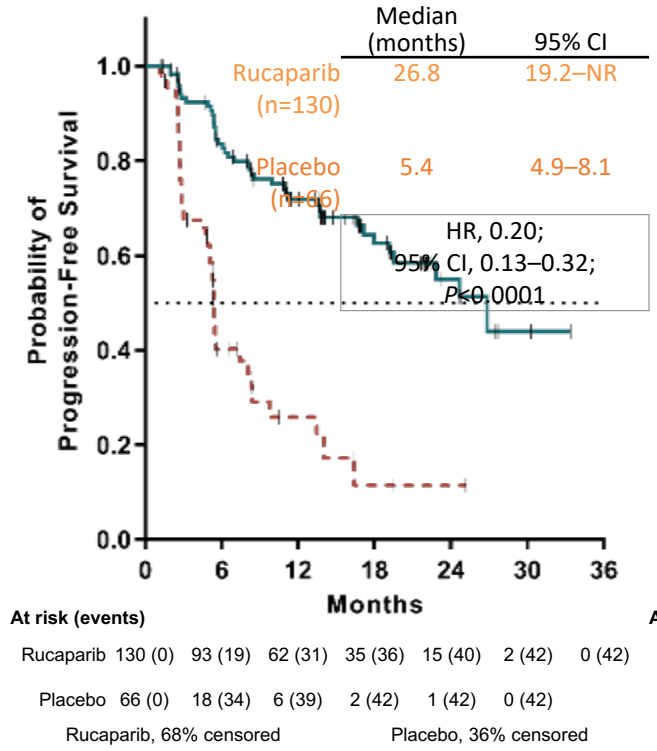
ARIEL3: BICR-Assessed Progression-Free Survival

BRCA mutant

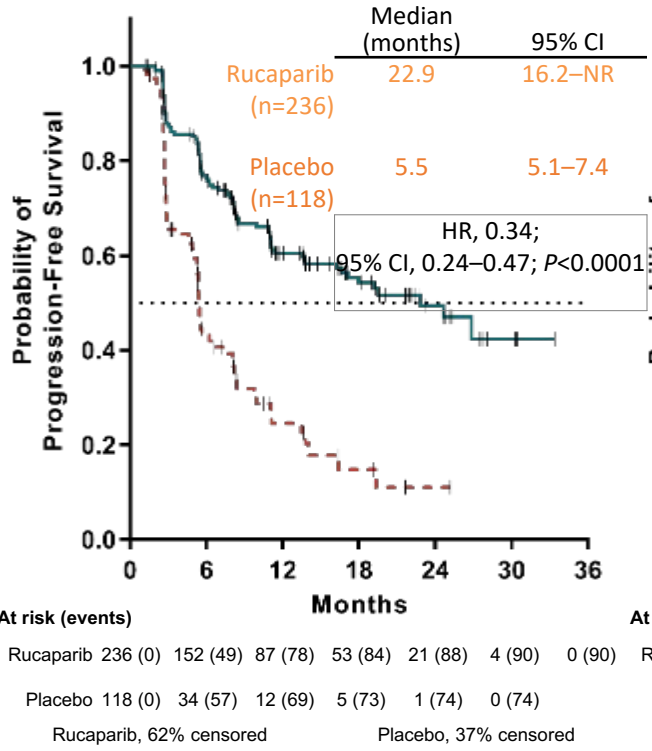


At risk (events)

Rucaparib	130 (0)	93 (19)	62 (31)	35 (36)	15 (40)	2 (42)	0 (42)
Placebo	66 (0)	18 (34)	6 (39)	2 (42)	1 (42)	0 (42)	

Rucaparib, 68% censored Placebo, 36% censored

HRD

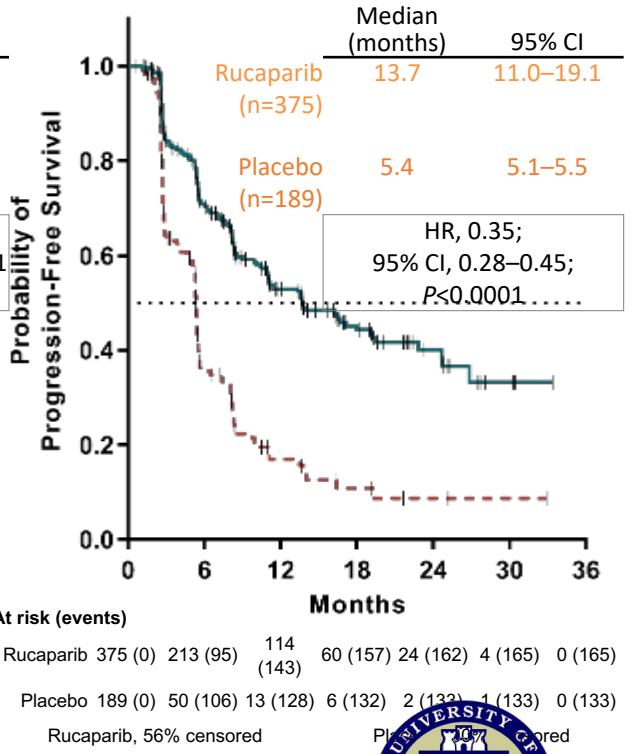


At risk (events)

Rucaparib	236 (0)	152 (49)	87 (78)	53 (84)	21 (88)	4 (90)	0 (90)
Placebo	118 (0)	34 (57)	12 (69)	5 (73)	1 (74)	0 (74)	

Rucaparib, 62% censored Placebo, 37% censored

ITT



At risk (events)

Rucaparib	375 (0)	213 (95)	114 (143)	60 (157)	24 (162)	4 (165)	0 (165)
Placebo	189 (0)	50 (106)	13 (128)	6 (132)	2 (133)	1 (133)	0 (133)

Rucaparib, 56% censored Pl[illegible]ored

[Lancet.](#) **2017 Oct 28;390(10106):1949-1961**

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PARP inhibitors treatment in recurrent ovarian cancer

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THE LANCET
Oncology

Rucaparib in relapsed, platinum-sensitive high-grade ovarian carcinoma (ARIEL2 Part 1): an international, multicentre, open-label, phase 2 trial

Elizabeth Swisher *et al* Lancet Oncol 2017; 18: 75–87

University of Pittsburgh

Study design

ARIEL2 is an international, multicentre, two-part, phase 2, open-label study.
Drug: Rucaparib, 600mg PO twice/day

Swisher, Lancet Oncol 2017; 18: 75–87

University of Pittsburgh

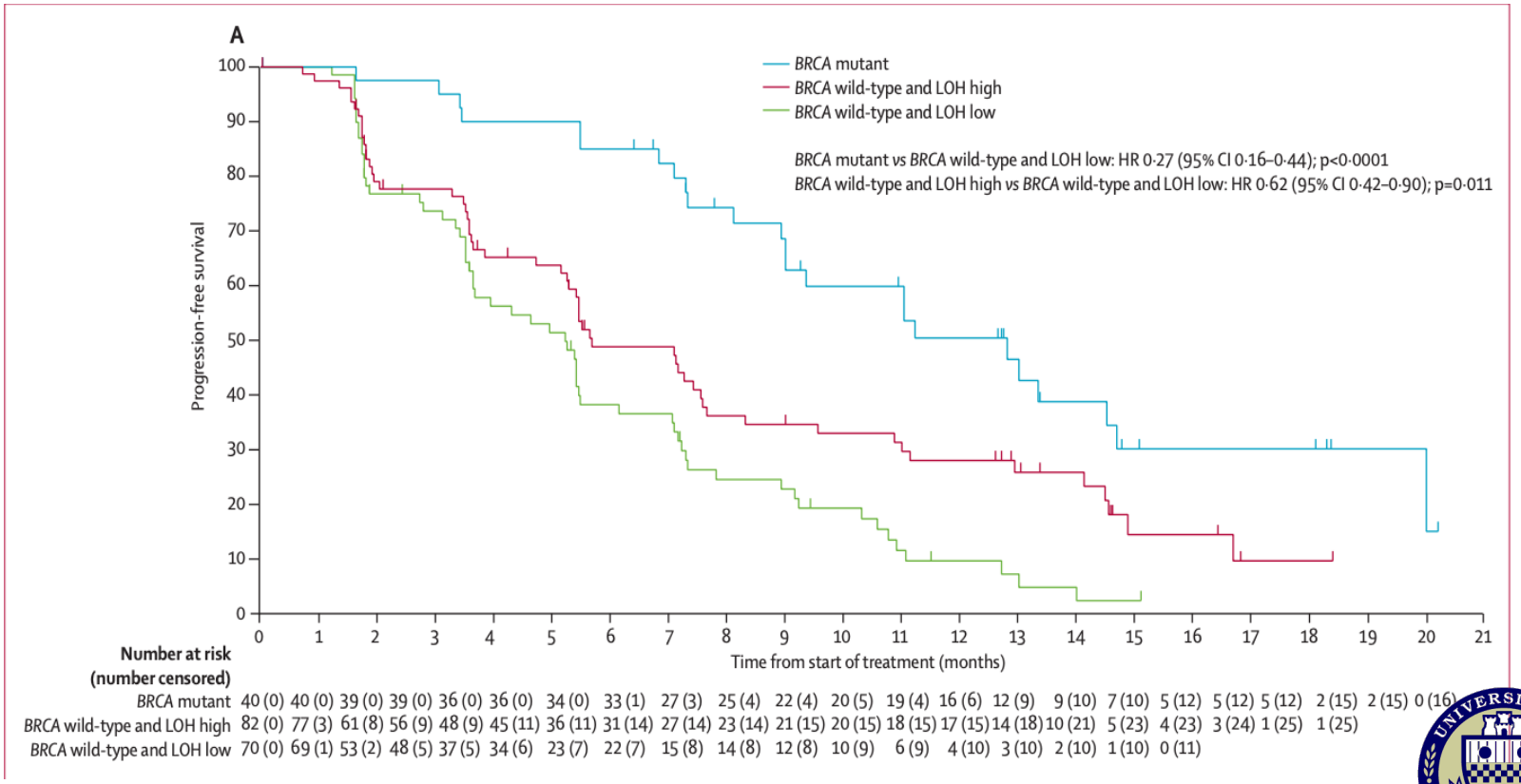
Result 1

- 192 treated patients could be classifi ed into one of the three subgroups: BRCA mutant (n=40), LOH high (n=82), or LOH low (n=70)
- Median PFS after rucaparib treatment was;
  - 12·8 months BRCA mutant subgroup
  - 5·7 months in the LOH high subgroup
  - 5·2 months in the LOH low subgroup

Swisher, Lancet Oncol 2017; 18: 75–87

University of Pittsburgh

Result 2



Swisher, Lancet Oncol 2017; 18: 75–87

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Olaparib Monotherapy versus Chemotherapy for Germline BRCA-Mutated Platinum-Sensitive Relapsed Ovarian Cancer Patients: Phase III SOLO3 Trial

Richard T Penson,[1] Ricardo Villalobos Valencia,[2] David Cibula,[3] Nicoletta Colombo,[4] Charles A Leath III,[5] Mariusz Bidziński,[6] Jae-Weon Kim,[7] Joo Hyun Nam,[8] Radoslaw Madry,[9] Carlos Hernández,[10] Paulo AR Mora,[11] Sang Young Ryu,[12] Tsveta Milenkova,[13] Elizabeth S Lowe,[14] Laura Barker,[13] Giovanni Scambia[15]

[1]Massachusetts General Hospital, Boston, MA, USA; [2]Centro Medico Dalinde, Mexico City, Mexico; [3]First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic; [4]University of Milan-Bicocca and IEO European Institute of Oncology IRCCS, Milan, Italy; [5]University of Alabama, Birmingham, AL, USA; [6]Faculty of Medicine and Health Sciences, Jan Kochanowski University, Kielce, Poland; [7]Seoul National University Hospital, Seoul, South Korea; [8]Asan Medical Center, Seoul, South Korea; [9]Medical University K. Marcinkowski and the Clinical Hospital of the Transfiguration, Poznań, Poland; [10]Oaxaca Site Management Organization, Oaxaca de Juarez, Mexico; [11]Instituto COI de Educação e Pesquisa, Rio de Janeiro, Brazil; [12]Korea Institute of Radiological and Medical Sciences, Seoul, South Korea; [13]AstraZeneca, Cambridge, UK; [14]AstraZeneca, Gaithersburg, MD, USA; [15]Università Cattolica del Sacro Cuore-Fondazione Policlinico A. Gemelli, IRCCS, Rome, Italy

ClinicalTrials.gov identifier: NCT02282020
This study was sponsored by AstraZeneca; part of an alliance between AstraZeneca and Merck & Co., Inc., Kenilworth, NJ, USA

Study Design

- Relapsed, high-grade serous or endometrioid ovarian, primary peritoneal, and/or fallopian tube cancer
- Germline BRCAm
- ECOG performance status 0–2
- ≥2 previous lines of platinum-based chemotherapy*
- Platinum sensitive†

Open-label

Study treatment administered until disease progression

Olaparib tablets 300 mg bid (n=178)

2:1 randomization

Stratified by:
- Selected chemotherapy‡
- Number of prior lines of chemotherapy
- Time to progression after previous platinum-based chemotherapy

Non-platinum chemotherapy§ (n=88)
- **PLD (n=47)**
- **Paclitaxel (n=20)**
- **Gemcitabine (n=13)**
- **Topotecan (n=8)**

Primary endpoint
- ORR by BICR (RECIST v1.1)

Secondary endpoints
- PFS
- PFS2
- OS
- TFST
- TSST
- HRQoL
- Safety

*Prior treatment with a PARP inhibitor was not permitted;
†Fully platinum sensitive: progression >12 months after platinum-based chemotherapy; partially platinum sensitive: progression 6–12 months after platinum-based chemotherapy;
‡For each patient, the investigator declared their choice of non-platinum chemotherapy before randomization;
§PLD, 50 mg/m² on day 1 q4w; paclitaxel, 80 mg/m² on days 1, 8, 15, and 22 q4w; gemcitabine, 1000 mg/m² on days 1, 8, and 15 q4w; topotecan, 4 mg/m² on days 1, 8, and 15 q4w
BICR, blinded independent central review; BRCAm, *BRCA1* or *BRCA2* mutation; ECOG, Eastern Cooperative Oncology Group; HRQoL, health-related quality of life; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, second progression-free survival; PLD, pegylated liposomal doxorubicin; q4w, every 4 weeks; RECIST, response evaluation criteria in solid tumors; TFST, time to first subsequent therapy or death; TSST, time to second subsequent therapy or death

Presented By Richard Penson at 2019 ASCO Annual Meeting

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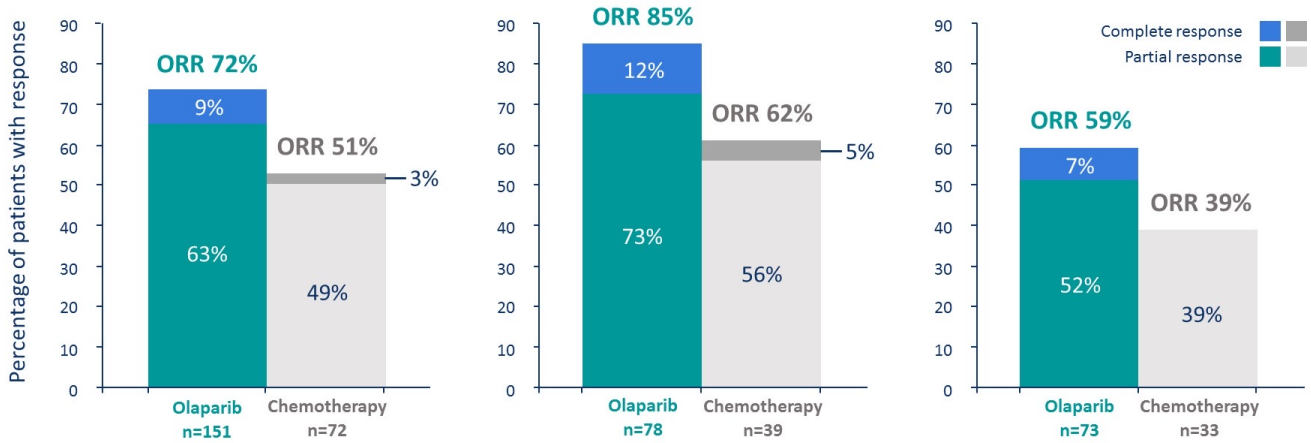
Primary Endpoint: ORR by BICR



All patients*
OR 2.53 (1.40, 4.58) *P*=0.002

Patients with 2 prior lines of chemotherapy*
OR 3.44 (1.42, 8.54)

Patients with ≥3 prior lines of chemotherapy*
OR 2.21 (0.96, 5.20)

*Patients with measurable disease at baseline

Presented By Richard Penson at 2019 ASCO Annual Meeting

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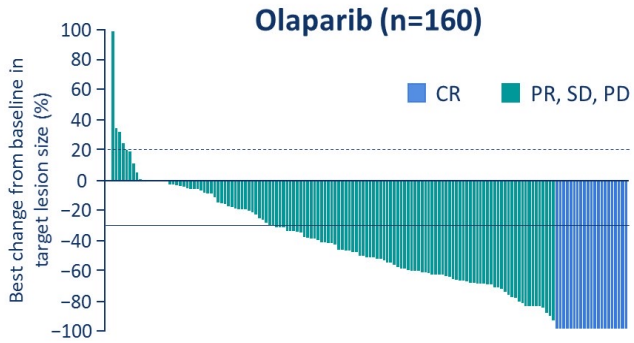
Investigator-Assessed Best Response for Target Lesions by Patient



	CR, n	PR, n	SD, n	PD, n	NE, n
Olaparib, n=160	21	83	39	6	11

	CR, n	PR, n	SD, n	PD, n	NE, n
PLD, n=44	3	23	11	0	7
Paclitaxel, n=17	0	5	7	2	3
Gemcitabine, n=10	0	1	4	0	5
Topotecan, n=7	0	1	1	1	4

CR, complete response; NE, not evaluable for investigator-assessed best response; PD, progressive disease; PR, partial response; SD, stable disease

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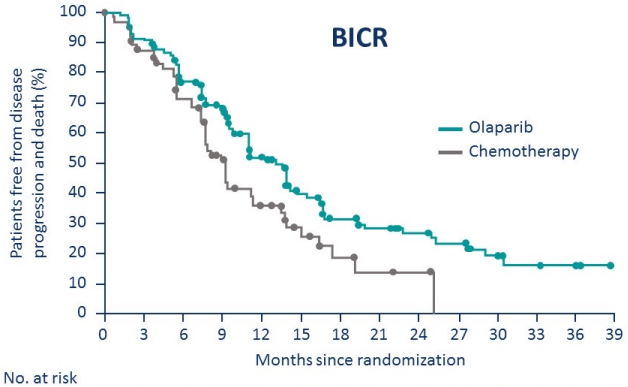
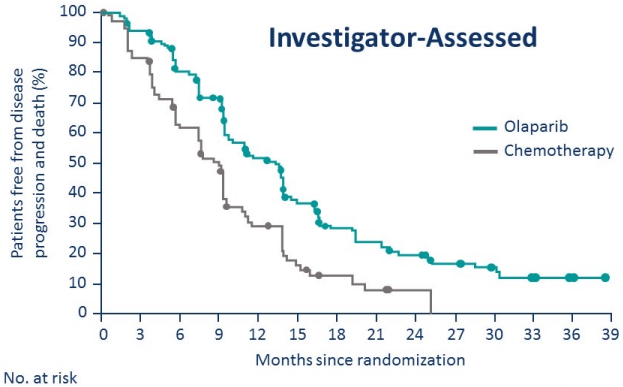
PFS (Intention-To-Treat Population)



No. at risk

Olaparib	178	156	126	108	71	47	30	25	18	14	8	5	2	0
Chemotherapy	88	63	47	31	18	9	5	3	2	0	0	0	0	0

	Olaparib (n=178)	Chemotherapy (n=88)
PFS events, n (%)	110 (62)	49 (56)
Median PFS, months	**13.4**	**9.2**
HR (95% CI), *P* value	**0.62 (0.43, 0.91); *P*=0.013**	



No. at risk

Olaparib	178	155	126	110	72	48	31	26	19	12	8	6	2	0
Chemotherapy	88	62	43	34	18	9	5	3	1	0	0	0	0	0

	Olaparib (n=178)	Chemotherapy (n=88)
PFS events, n (%)	123 (69)	63 (72)
Median PFS, months	**13.2**	**8.5**
HR (95% CI), *P* value	**0.49 (0.35, 0.70); *P*<0.001**	

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PARP inhibitors maintenance after 1st line treatment of ovarian cancer

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SOLO1: Phase III trial of maintenance olaparib following platinum-based chemotherapy in newly diagnosed patients with advanced ovarian cancer and a *BRCA1/2* mutation

- Kathleen Moore,[1] Nicoletta Colombo,[2] Giovanni Scambia,[3] Byoung-Gie Kim,[4] Ana Oaknin,[5] Michael Friedlander,[6]
  Alla Lisyanskaya,[7] Anne Floquet,[8] Alexandra Leary,[9] Gabe S. Sonke,[10] Charlie Gourley,[11] Susana Banerjee,[12] Amit Oza,[13] Antonio González-Martín,[14] Carol Aghajanian,[15] William Bradley,[16] Elizabeth S. Lowe,[17] Ralph Bloomfield,[18] Paul DiSilvestro[19]

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ESMO Congress, Munich 2018

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
- Cytoreductive surgery*
- In clinical complete response or partial response after platinum-based chemotherapy

Olaparib 300 mg bd (N=260)

2:1 randomization

Stratified by response to platinum-based chemotherapy

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

2 years' treatment if no evidence of disease

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 randomization 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; 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; PFS, progression-free survival; PFS2, time to second progression or death; RECIST, Response Evaluation Criteria in Solid Tumours; TOI, Trial Outcome Index

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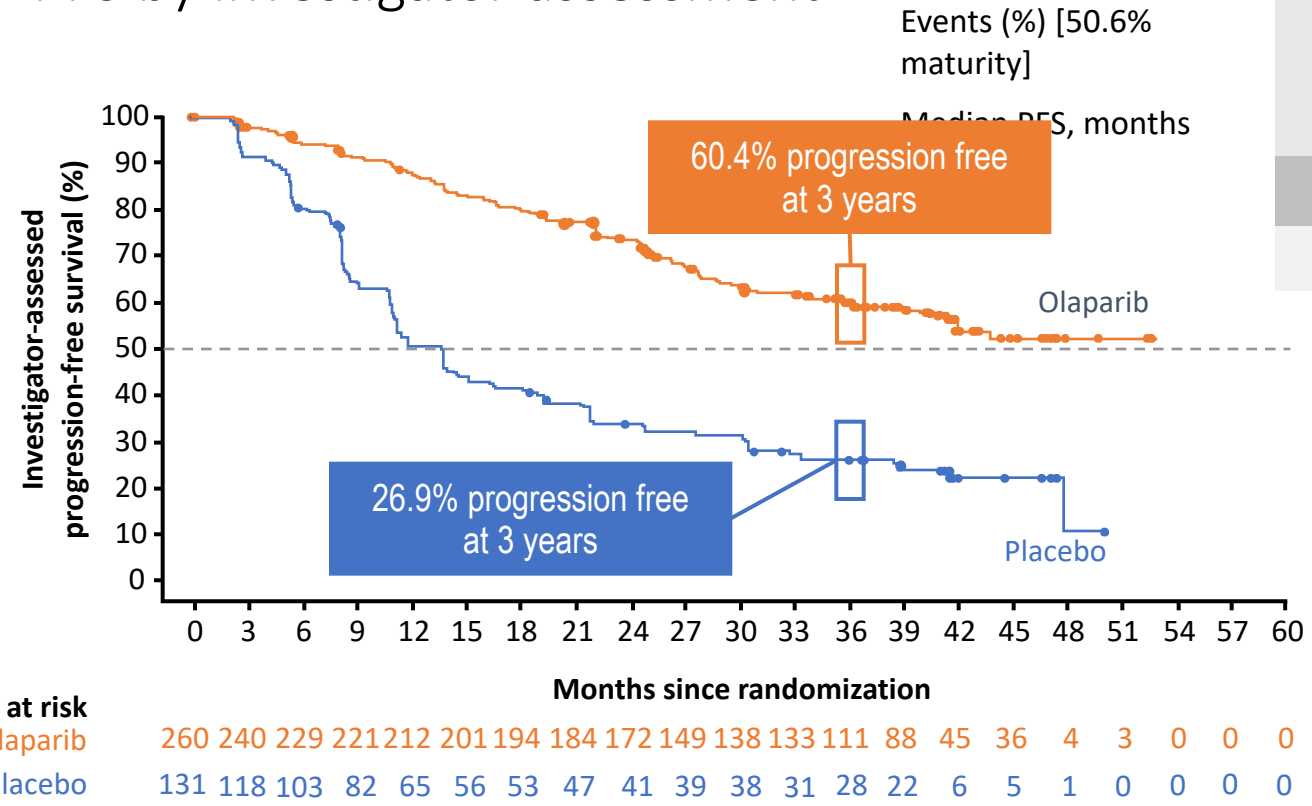
PFS by investigator assessment



	Olaparib (N=260)	Placebo (N=131)
Events (%) [50.6% maturity]	102 (39.2)	96 (73.3)
Median PFS, months	NR	13.8
HR 0.30		
95% CI 0.23, 0.41; *P*<0.0001		

No. at risk																				
Olaparib	260	240	229	221	212	201	194	184	172	149	138	133	111	88	45	36	4	3	0	0	0
Placebo	131	118	103	82	65	56	53	47	41	39	38	31	28	22	6	5	1	0	0	0	0

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CI, confidence interval; NR, not reached

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Niraparib Therapy in Patients With Newly Diagnosed Advanced Ovarian Cancer (PRIMA/ENGOT-OV26/GOG-3012)

A. González-Martín,[1] B. Pothuri,[2] I. Vergote,[3] R.D. Christensen,[4] W. Graybill,[5] M.R. Mirza,[6] C. McCormick,[7] D. Lorusso,[8] P. Hoskins,[9] G. Freyer,[10] F. Backes,[11] K. Baumann,[12] A. Redondo,[13] R. Moore,[14] C. Vulsteke,[15] R.E. O'Cearbhaill,[16] B. Lund,[17] Y. Li,[18] D. Gupta,[18] B.J. Monk[19]

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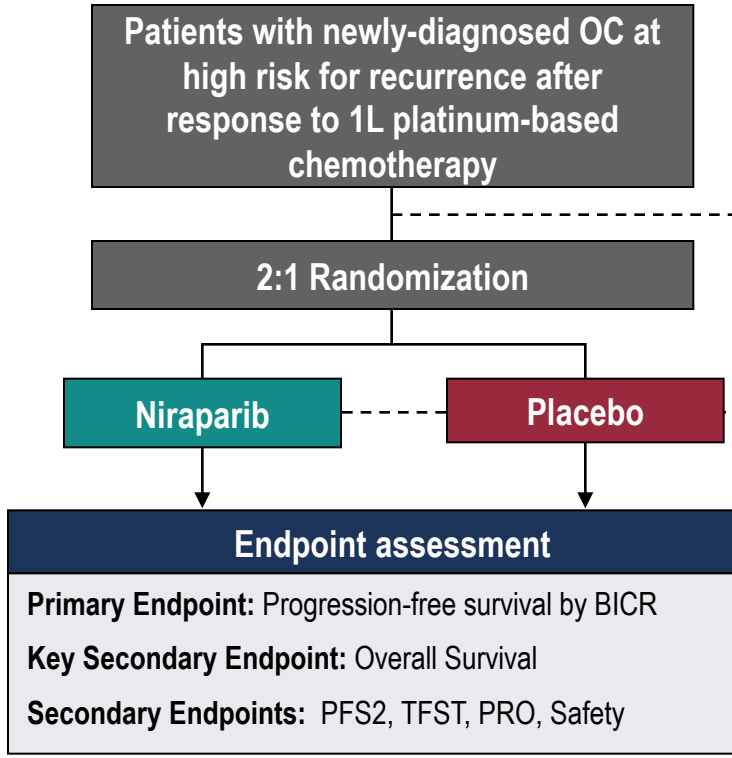
PRIMA Trial Design



Patients were treated with niraparib or placebo once daily for 36 months or until disease progression

Stratification Factors

- Neoadjuvant chemotherapy administered: Yes or no
- Best response to first platinum therapy: CR or PR
- Tissue homologous recombination test status: deficient or proficient/not-determined

- Body weight ≥77 kg and platelets ≥150,000/µL started with 300 mg QD
- Body weight <77 kg and/or platelets <150,000/µL started with 200

Hierarchical PFS Testing

- **Patients with homologous recombination deficient tumors**, followed by the **overall population**.
- Statistical assumption: a hazard ratio benefit in PFS of
  - 0.5 in homologous recombination deficient patients
  - 0.65 in the overall population
- >90% statistical power and one-sided type I error of 0.025

1L, first-line; BICR, blinded independent central review; CR, complete response; OC, ovarian cancer; PFS2, progression-free survival 2; PR partial response; PRO, patient-reported outcomes; TFST, time to first subsequ[illegible]apy.

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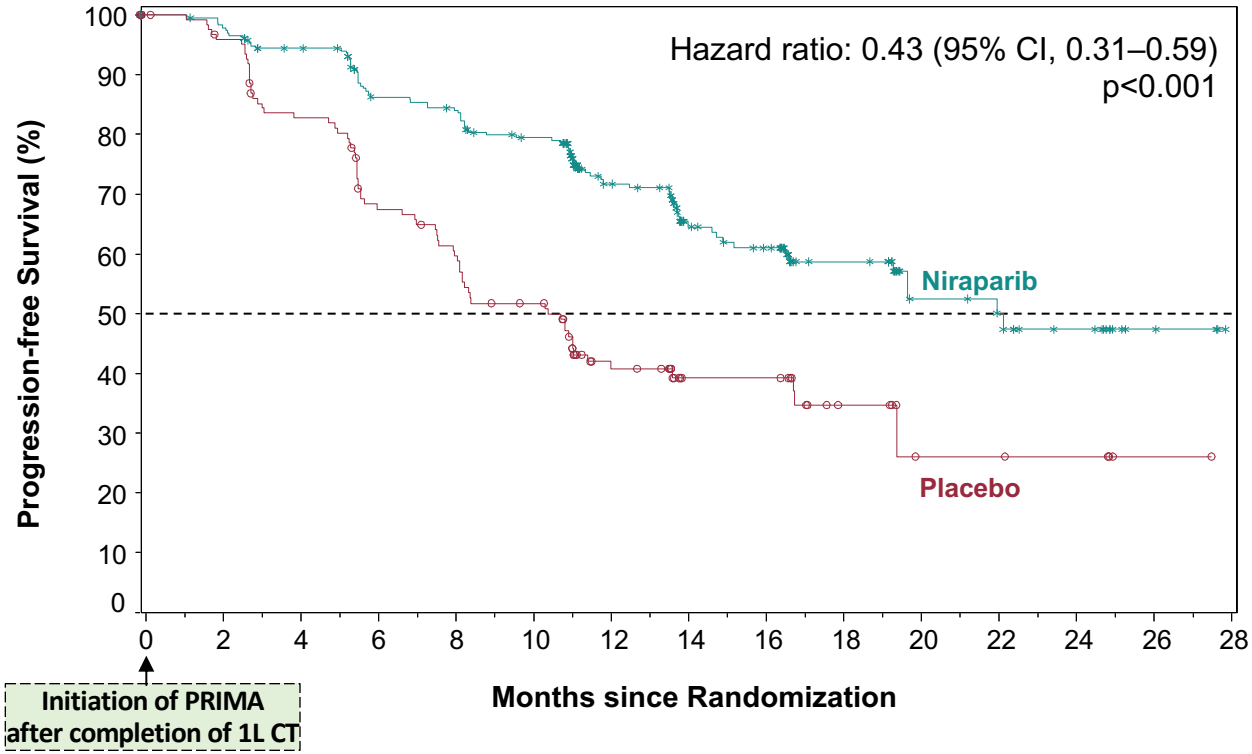
PRIMA Primary Endpoint, PFS Benefit in the HR-deficient Population



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.

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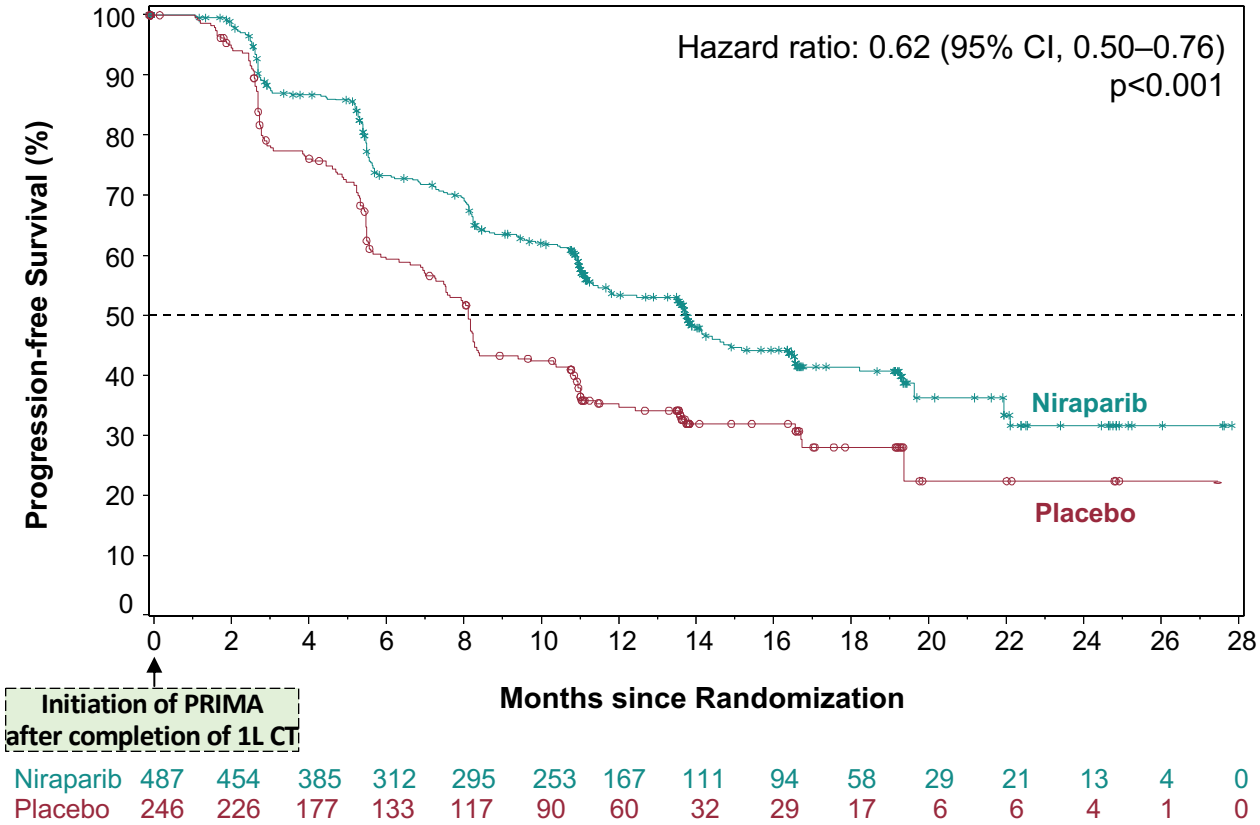
PRIMA Primary Endpoint, PFS Benefit in the Overall Population



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%.

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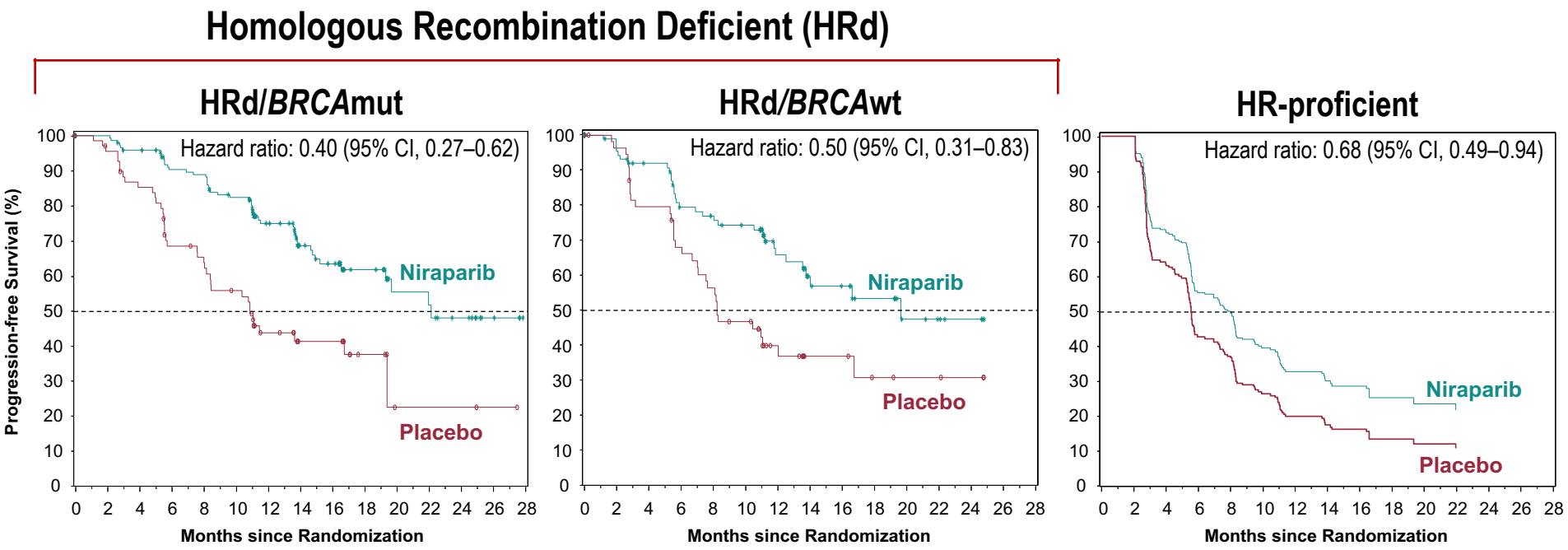
PRIMA PFS Benefit in Biomarker Subgroups



- Niraparib provided similar clinical benefit in the HRd subgroups (*BRCA*mut and *BRCA*wt)
- Niraparib provide clinically significant benefit in the HR-proficient subgroup with a 32% risk reduction in progression or death

CI, confidence interval; HR, homologous recombination; mut, mutation; PFS, progression-free survival wt, wild-type.

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Phase III PAOLA-1/ENGOT-ov25: maintenance olaparib with bevacizumab in patients with newly diagnosed, advanced ovarian cancer treated with platinum-based chemotherapy and bevacizumab as standard of care

Isabelle Ray-Coquard, Patricia Pautier, Sandro Pignata, David Pérol, Antonio González-Martin, Paul Sevelda, Keiichi Fujiwara, Ignace Vergote, Nicoletta Colombo, Johanna Mäenpää, Frédéric Selle, Jalid Sehouli, Domenica Lorusso, Eva Maria Guerra Alia, Claudia Lefeuvre-Plesse, Ulrich Canzler, Alain Lortholary, Frederik Marmé, Eric Pujade-Lauraine, Philipp Harter

ClinicalTrials.gov identifier: NCT02477644
This study was sponsored by ARCAGY Research

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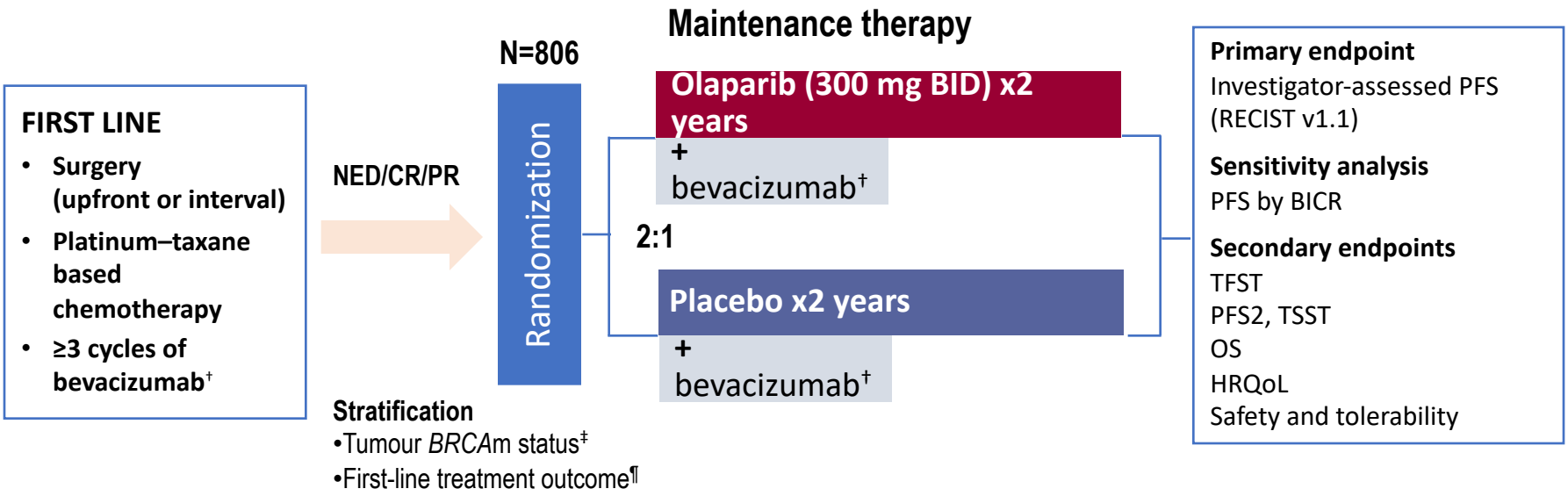
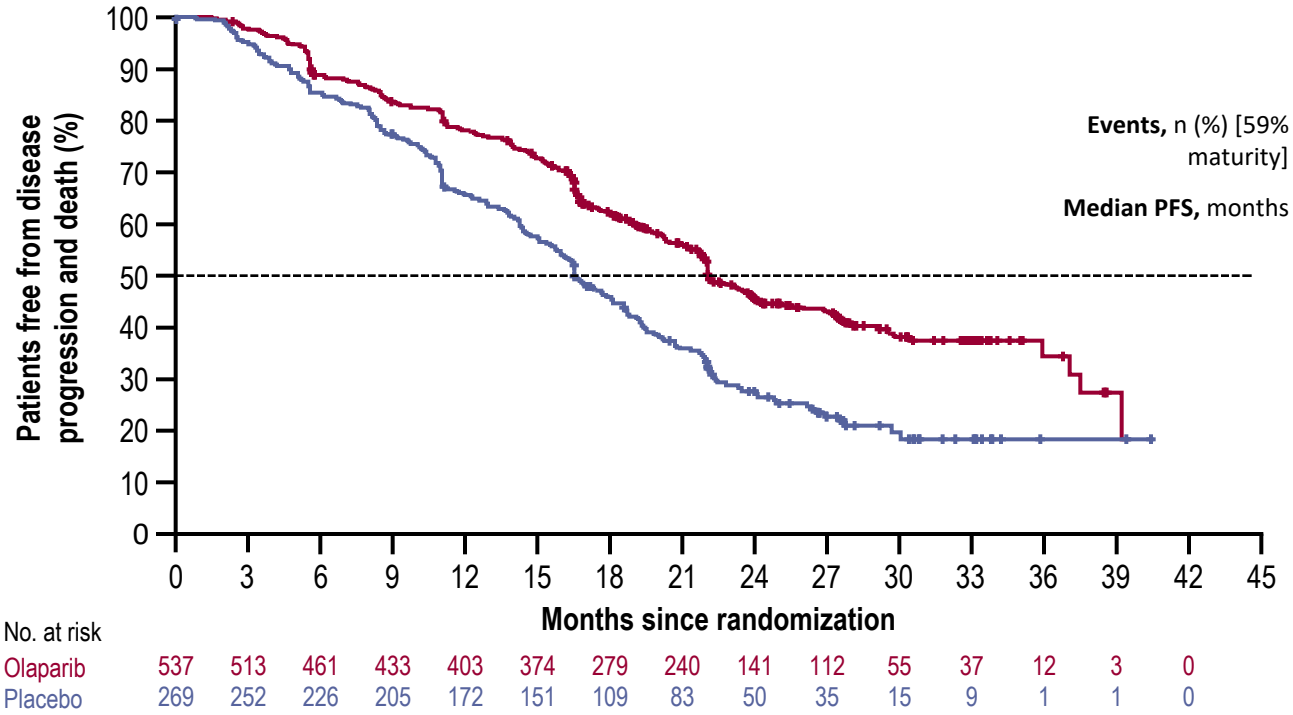
Study design

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
BICR, blinded independent central review; HRQoL, health-related quality of life; PFS2, time to second progression or death; RECIST, Response Evaluation Criteria in Solid Tumours; TFST, time to first subsequent therapy or death; TSST, time to second subsequent therapy or death

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

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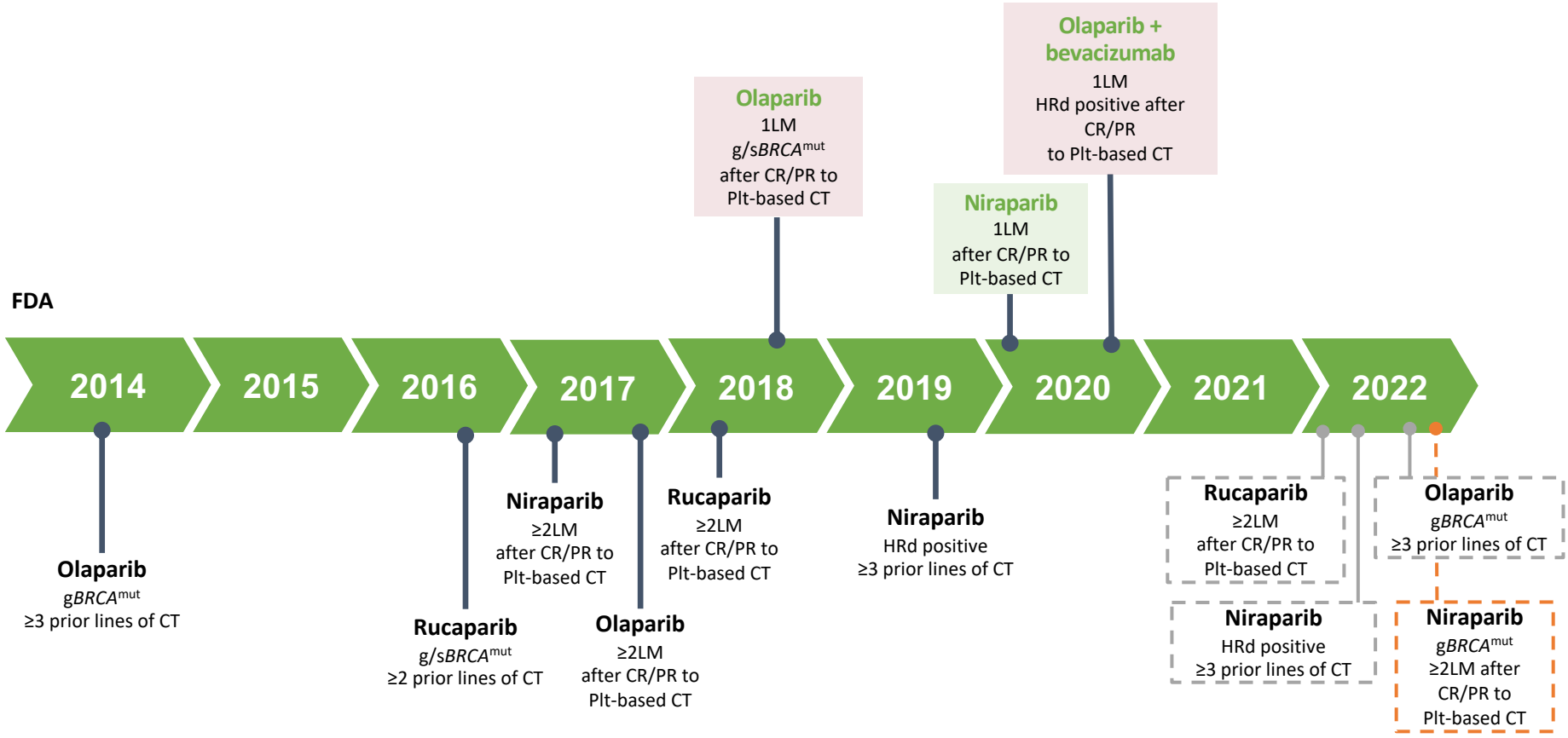
FDA Approvals of PARPi in Ovarian Cancer



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Conclusions

- **Carboplatin and paclitaxel doublet remains the backbone of initial ovarian cancer therapy.**
- **When ovarian cancer becomes platinum resistant, the patient is in trouble.**
- **Multiple molecular targets have been modulated for the treatment of recurrent ovarian cancer with varying degrees of success.**
- **Enrollment/participation should be the prime goal for recurrent ovarian cancer therapy at this time.**

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Thank you!