Breakfast with the Investigators:
New Agents and Strategies in the Management of Ovarian Cancer

Sunday, June 4, 2017
6:45 AM – 7:45 AM
Chicago, Illinois

Faculty

Michael Birrer, MD, PhD
Joyce F Liu, MD, MPH
Mansoor Raza Mirza, MD

Moderator

Neil Love, MD

Research To Practice®

Disclosures for Moderator Neil Love, MD

Dr Love is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma, Agendia Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Medivation Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology and Tokai Pharmaceuticals Inc.

Agenda

BRCA and Other Potential Genetic Drivers of Ovarian Cancer Development

Integration of Approved PARP Inhibitors into Ovarian Cancer Treatment Algorithms

Treatment Options for Platinum-Sensitive Recurrent Disease

Promising Investigational Strategies

What are the iPads® for?

To enable you to more fully participate in the meeting

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.

Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

Complete Your Evaluation: Tap the CME Evaluation button to complete your evaluation electronically to receive credit for your participation.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

About the Enduring Program

- This live meeting is being video recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.

- An email will be sent to all attendees when the activity is available.
- To learn more about our education programs visit our website, www.ResearchToPractice.com

Make the Meeting Even More Relevant to You

Download the RTPLive app on your smartphone or tablet to access program information, including slides being presented during the program:

www.ResearchToPractice.com/RTPLiveApp

Breakfast with the Investigators:
New Agents and Strategies in the Management of Ovarian Cancer

Sunday, June 4, 2017
6:45 AM – 7:45 AM
Chicago, Illinois

Faculty

Michael Birrer, MD, PhD
Joyce F Liu, MD, MPH
Mansoor Raza Mirza, MD

Moderator

Neil Love, MD

Research To Practice®

A 46 yo woman is s/p debulking surgery for a stage 3C, high-grade serous OC. She received carbo/paclitaxel and was in clinical CR for 14 months when recurrent disease was found in para-aortic and mediastinal nodes. Which treatment would you likely recommend if she was….

- BRCA germline mutation-positive
- BRCA somatic mutation-positive
- BRCA wild type

ARTICLE IN PRESS

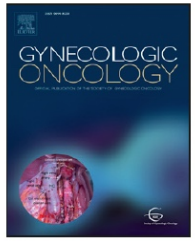
YGYNO-976695; No. of pages: 5; 4C:

Gynecologic Oncology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno



Clinical Commentary

Poly(ADP-ribose) polymerase (PARP) inhibitors as treatment versus maintenance in ovarian carcinoma

Whitney S. Graybill
Medical University of South Carolina, Hollings Cancer Center, 86 Jonathan Lucas Street, Charleston, SC 29425, United States

Bhavana Pothuri
Department of Obstetrics and Gynecology, NYU Langone Medical Center, 240 East 38th Street, 19th Floor, New York, NY 10016, United States

Dana M. Chase
Bradley J. Monk*
Division of Gynecologic Oncology, Arizona Oncology (US Oncology Network), University of Arizona College of Medicine, Creighton University School of Medicine at St. Joseph's Hospital, 2222 E. Highland Avenue, Suite 400, Phoenix, AZ 85016, United States
*Corresponding author.
E-mail address: Bradley.monk@usoncology.com (B.J. Monk).

Phase III Studies of Bevacizumab in Combination with Chemotherapy for EOC: Platinum-Sensitive, Recurrent Setting

Study	Randomization	N	Median PFS (mo)	HR, *p*-value	Median OS (mo)	HR, *p*-value
OCEANS[1]	C/gem + placebo C/gem + bev until progression	242 242	8.4 12.4	HR = 0.48 <0.0001	32.9 33.6	HR = 0.952 0.6479
GOG-0213[2]	C/P C/P + bev	374 374	10.4 13.8	HR = 0.628 <0.0001	37.3 42.2	HR = 0.829 0.056

[1] Aghajanian C et al. *J Clin Oncol* 2012;30(17):2039-45; *Gynecol Oncol* 2015;139(1):10-6.
[2] Coleman RL et al. *Lancet Oncol* 2017 April 21;[Epub ahead of print].

Case 1 (Dr Mirza)

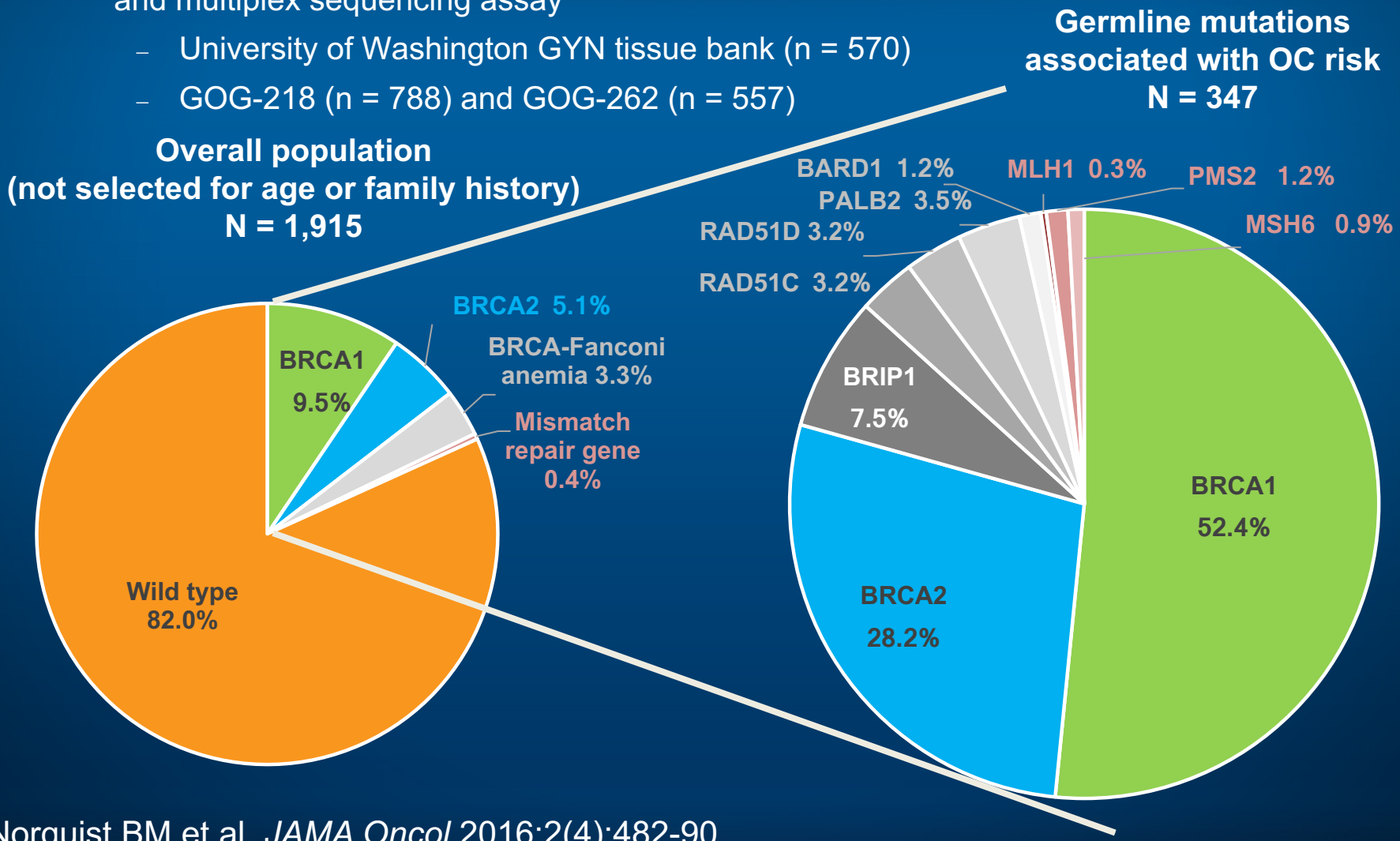
- 2012: 46 yo old woman with BRCA1 germline mutation diagnosed with high-grade serous stage IV OC
- Not optimal primary debulking surgery, with residual disease (mediastinum, porta hepatis)
- 6 courses of concomitant carbo-pac-bev (achieved CR) -> maintenance bevacizumab
- Relapse (mediastinum + para-aortic) at 14th month of maintenance bevacizumab
- 6 courses of carboplatin-PLD (achieved CR)
- Oct 2013: Maintenance Olaparib (due to toxicity dose reduced to 200mg BID)
- Nov 2015: Slight increase in CA-125, no progression on PET-CT – Olaparib dose increased to 400mg x 2
- Jan 2016: Neurological symptoms – MR – multiple CNS mets; no extracranial relapse. Olaparib paused

Case 1 (Dr Mirza - Continued)

- Stereotactic Radiosurgery plus temozolomide + pembrolizumab + ipilimumab; considerable toxicity
- May 2016: Olaparib 200mg BID re-challenge
- February 2017: Slight elevation of CA-125 > carboplatin + veliparib: CR, but tx held after 3 courses due to excessive toxicity
- Patient is currently in the Caribbean enjoying time with her husband and two children

Summary of Germline DNA Mutations in OC

- Germline DNA sequenced from women with OC (N = 1,915) using a targeted capture and multiplex sequencing assay
  - University of Washington GYN tissue bank (n = 570)
  - GOG-218 (n = 788) and GOG-262 (n = 557)



Norquist BM et al. *JAMA Oncol* 2016;2(4):482-90.

Frey and Pothuri *Gynecologic Oncology Research and Practice* (2017) 4:4
DOI 10.1186/s40661-017-0039-8

Gynecologic Oncology Research and Practice

REVIEW Open Access

Homologous recombination deficiency (HRD) testing in ovarian cancer clinical practice: a review of the literature

Melissa K. Frey[1] and Bhavana Pothuri[2*]

FDA Approval of Olaparib (12/20/14)

- In pts with deleterious or suspected deleterious germline BRCA-mutated advanced recurrent ovarian cancer who have received 3 or more prior lines of chemotherapy
- Recommended dose is 400 mg PO BID
- Dose reductions to 200 mg PO BID and 100 mg PO BID can be used if necessary
- The indication was approved under accelerated approval based on objective response rate and duration of response based on Kaufman et al *JCO* 2015

Courtesy of Ursula Matulonis, MD

Olaparib in Germline BRCA1/2 Mutation-Positive Advanced Ovarian Cancer

- N = 137
- Deleterious or suspected deleterious germline BRCA mutation status verified retrospectively in 59/61 (97%) patients for whom blood samples were available, using the companion diagnostic BRACAnalysis CDx
- All patients had received 3 or more prior lines of chemotherapy
- All patients received olaparib 400 mg twice daily until disease progression or unacceptable toxicity
- Objective response rate: 34%
  - Complete response: 2%
  - Partial response: 32%
- Median DOR: 7.9 months

Olaparib package insert.

Adverse Events Reported in ≥20% of Patients with Germline BRCA Mutation-Positive OC Who Received 3 or More Lines of Prior Chemotherapy

Adverse event	N = 223	
	Any grade	Grade 3 or 4
Fatigue/asthenia	66%	8%
Anemia	34%	18%
Abdominal pain/discomfort	43%	8%
Decreased appetite	22%	1%
Nausea	64%	3%
Vomiting	43%	4%
Diarrhea	31%	1%
Dyspepsia	25%	0%

AE-related treatment discontinuation: 7%

Olaparib package insert.

Press Release – December 19, 2016
Accelerated Approval for Rucaparib

"The US Food and Drug Administration today granted accelerated approval to rucaparib for women with advanced ovarian cancer who have been treated with two or more chemotherapies and whose tumors have a specific gene mutation (deleterious BRCA) as identified by an FDA-approved companion diagnostic test.

"…the FDA also approved the FoundationFocus CDxBRCA companion diagnostic for use with rucaparib, which is the first next-generation-sequencing (NGS)-based companion diagnostic approved by the agency. The NGS test detects the presence of deleterious BRCA gene mutations in the tumor tissue of ovarian cancer patients."

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm533873.htm

Rucaparib in Germline and/or Somatic BRCA1/2 Mutation-Positive Advanced Ovarian Cancer

- N = 106 in 2 multicenter, single-arm, open-label clinical trials
- Tumor BRCA mutation status was verified retrospectively in 64/67 (96%) patients for whom a tumor tissue sample was available, using the companion diagnostic FoundationFocus CDx_{BRCA} test
- All patients had received 2 or more prior lines of chemotherapy
- All patients received rucaparib 600 mg twice daily as monotherapy until disease progression or unacceptable toxicity
- Objective response rate: 54%
  - Complete response: 9%
  - Partial response: 45%
- Median DOR: 9.2 months

Rucaparib package insert.

Rucaparib-Associated Adverse Events (N = 377)

Adverse event	All grades	Grade 3/4
Asthenia/fatigue	77%	11%
Nausea	77%	5%
Vomiting	46%	4%
Anemia	44%	25%
ALT/AST increased	41%	11%
Constipation	40%	2%
Decreased appetite	39%	3%
Dysgeusia	39%	<1%
Diarrhea	35%	2%
Abdominal pain	32%	3%
Thrombocytopenia	21%	5%

Treatment-related AE leading to discontinuation: 8%

Kristeleit RS et al. *Proc ESMO* 2016;Abstract 856O.

The poly(ADP-ribose) polymerase inhibitor niraparib (MK4827) in *BRCA* mutation carriers and patients with sporadic cancer: a phase 1 dose-escalation trial

Shahneen K Sandhu, William R Schelman, George Wilding, Victor Moreno, Richard D Baird, Susana Miranda, Lucy Hylands, Ruth Riisnaes, Martin Forster, Aurelius Omlin, Nathan Kreischer, Khin Thway, Heidrun Gevensleben, Linda Sun, John Loughney, Manash Chatterjee, Carlo Toniatti, Christopher L Carpenter, Robert Iannone, Stan B Kaye, Johann S de Bono, Robert M Wenham

Lancet Oncol **2013; 14: 882–92**

The NEW ENGLAND JOURNAL of MEDICINE

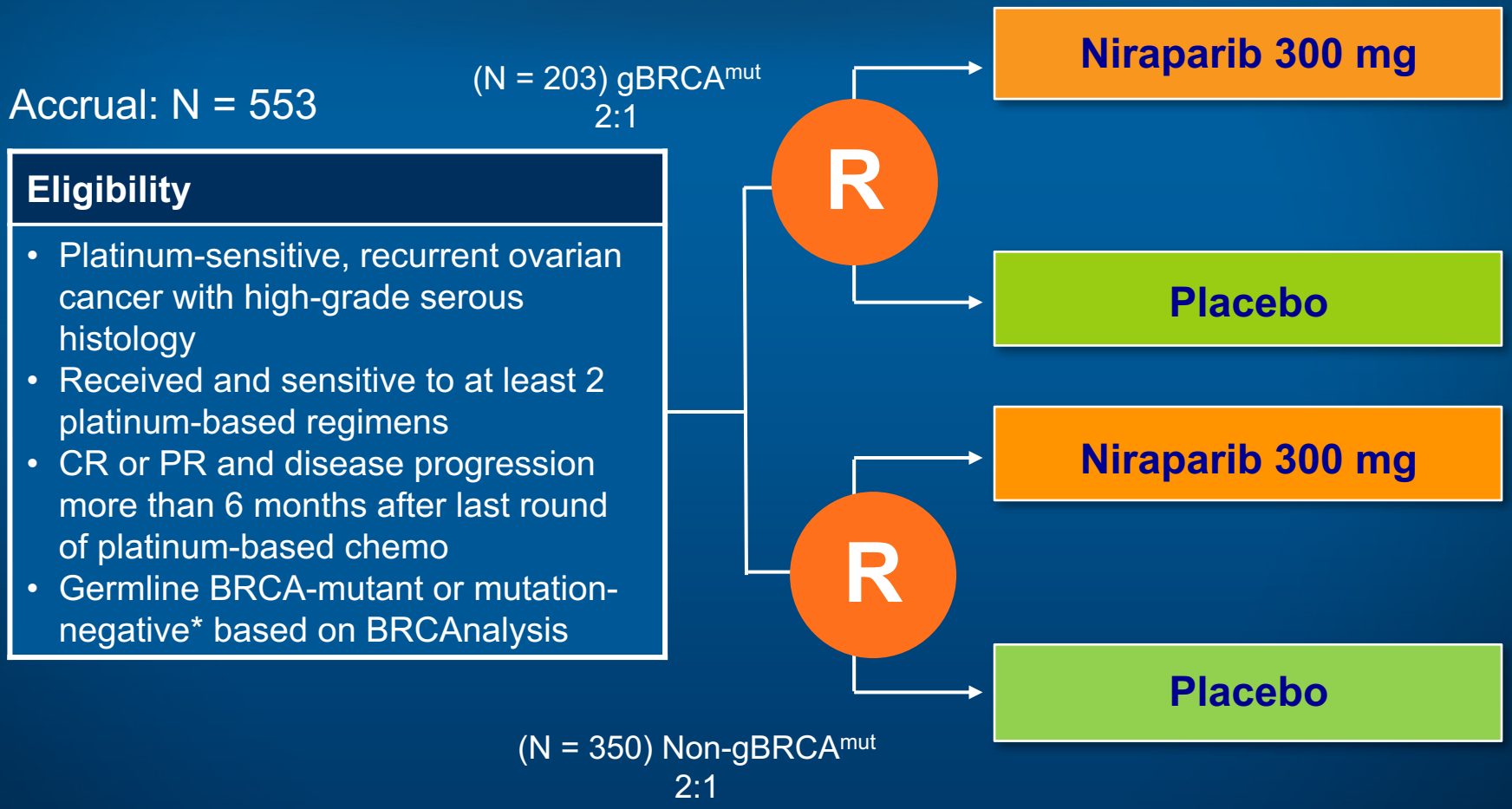
ORIGINAL ARTICLE

Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer

M.R. Mirza, B.J. Monk, J. Herrstedt, A.M. Oza, S. Mahner, A. Redondo, M. Fabbro, J.A. Ledermann, D. Lorusso, I. Vergote, N.E. Ben-Baruch, C. Marth, R. Mądry, R.D. Christensen, J.S. Berek, A. Dørum, A.V. Tinker, A. du Bois, A. González-Martín, P. Follana, B. Benigno, P. Rosenberg, L. Gilbert, B.J. Rimel, J. Buscema, J.P. Balser, S. Agarwal, and U.A. Matulonis, for the ENGOT-OV16/NOVA Investigators*

N Engl J Med 2016;375(22):2154-64.

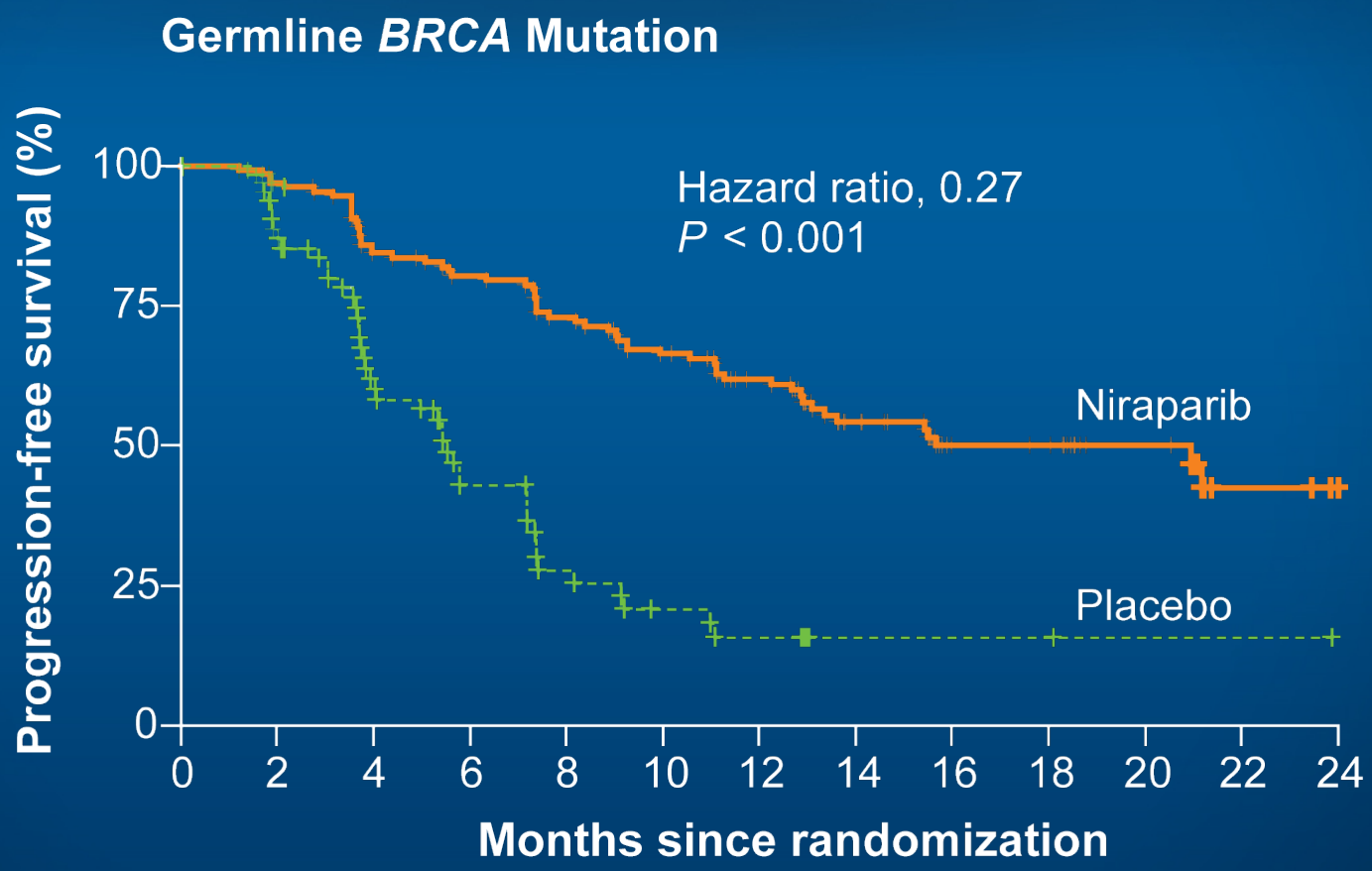
ENGOT-OV16/NOVA Schema



Primary endpoint: PFS in gBRCAmut and non-gBRCAmut cohorts (HRD-positive subset followed by overall)

Mirza MR et al. *N Engl J Med* 2016;375(22):2154-64; *Proc ESMO* 2016;Abstract LBA3_PR.

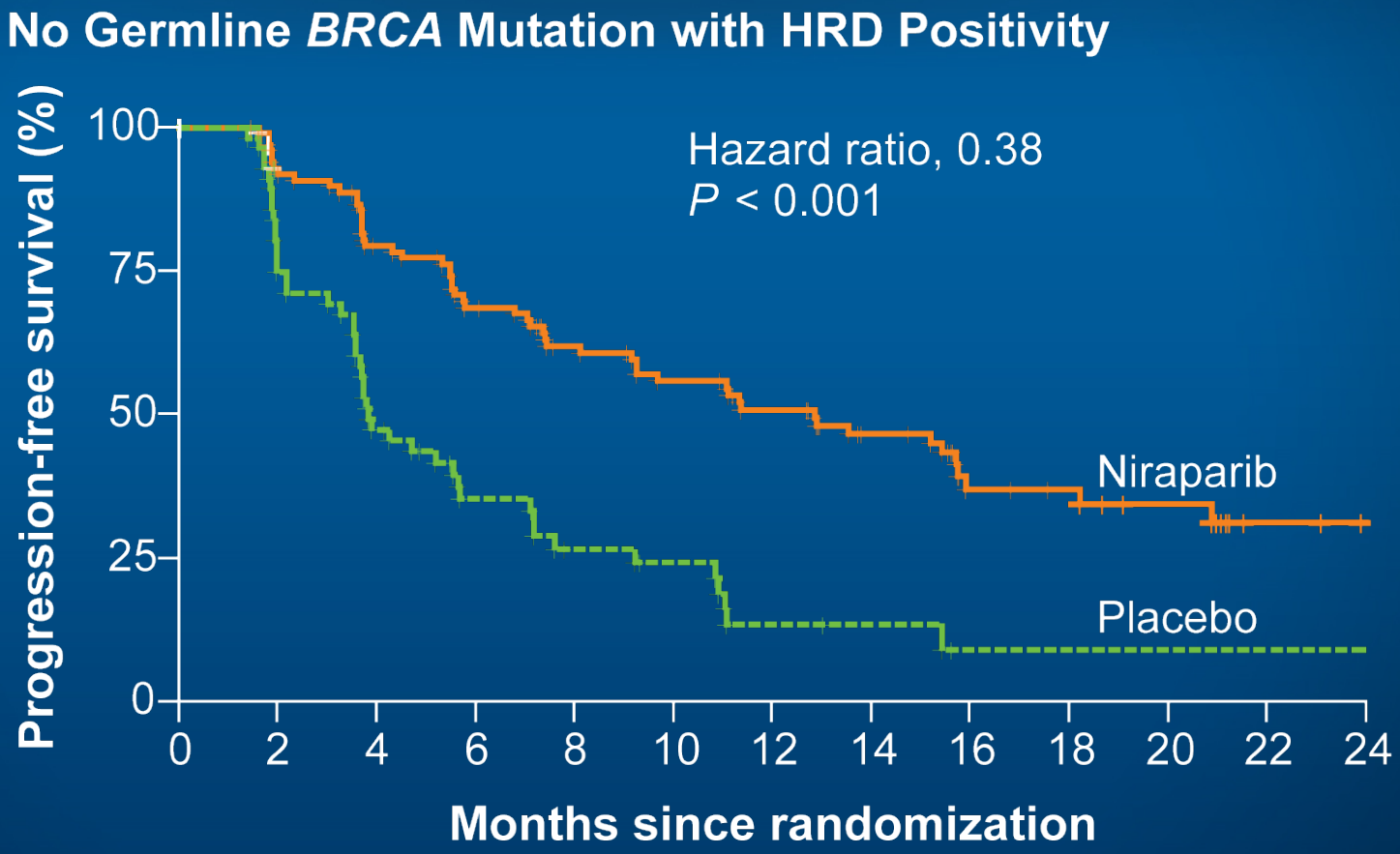
ENGOT-OV16/NOVA: PFS for gBRCA Mutation



No. at Risk													
Niraparib	138	125	107	98	89	79	63	44	28	26	16	3	1
Placebo	65	52	34	21	12	8	6	2	2	2	1	1	0

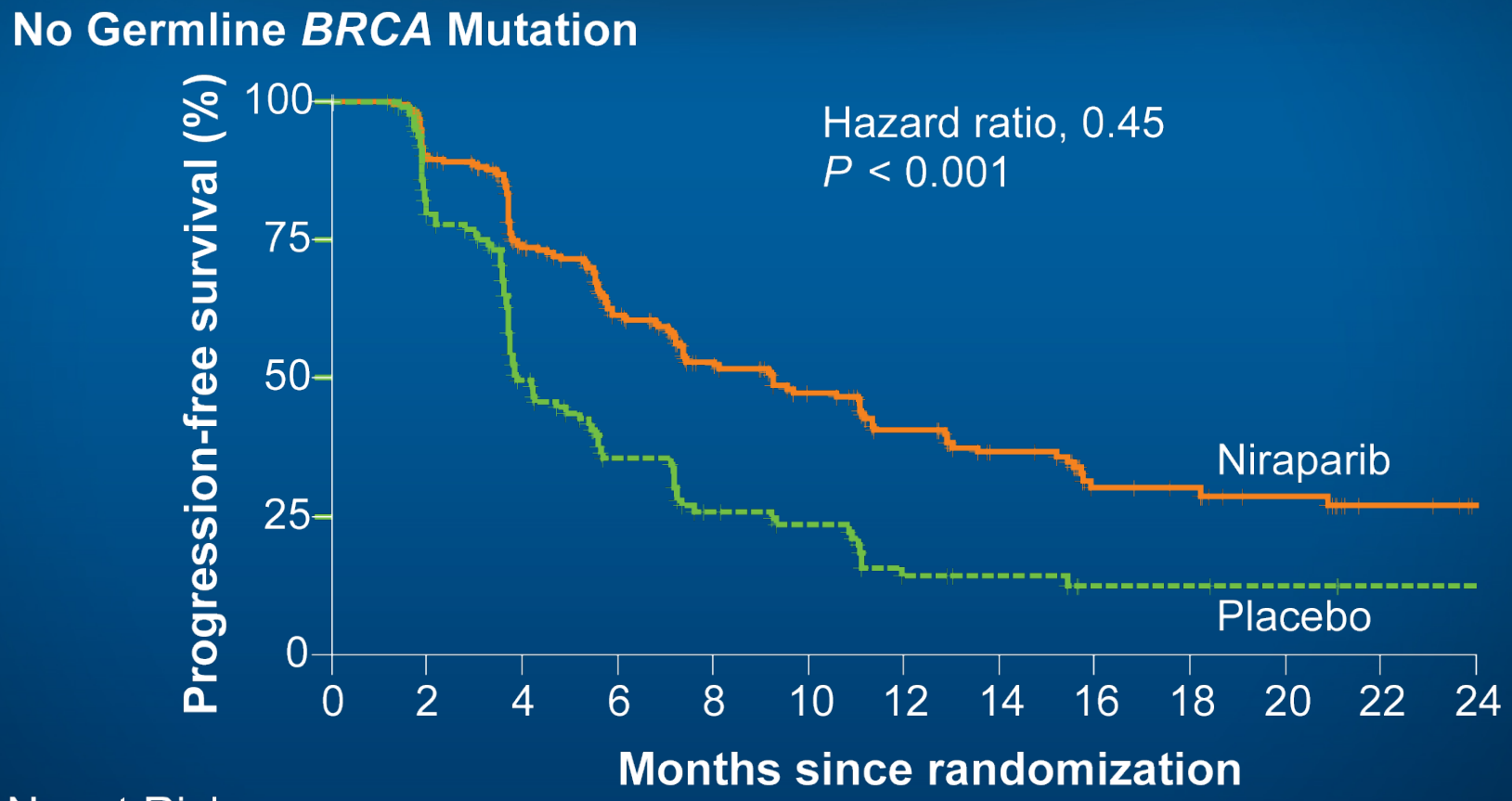
Mirza MR et al. *N Engl J Med* 2016; 375(22):2154-64

ENGOT-OV16/NOVA: PFS for No gBRCA Mutation with HRD Positivity



Mirza MR et al. *N Engl J Med* 2016; 375(22):2154-64

ENGOT-OV16/NOVA: PFS for No gBRCA Mutation



Mirza MR et al. *N Engl J Med* 2016; 375(22):2154-64

ENGOT-OV16/NOVA: Progression-Free Survival

Median PFS	Niraparib	Placebo	Hazard ratio	*p*-value
Germline BRCA Mutation (n = 138, 65)	21.0 mo	5.5 mo	0.27	<0.001
No Germline BRCA Mutation with HRD Positivity (n = 106, 56)	12.9 mo	3.8 mo	0.38	<0.001
No Germline BRCA Mutation (n = 234, 116)	9.3 mo	3.9 mo	0.45	<0.001

Mirza MR et al. *N Engl J Med* 2016; 375(22):2154-64

ENGOT-OV16/NOVA: Select Adverse Events

Event	Niraparib (N = 367)		Placebo (N = 179)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Fatigue	59.4%	8.2%	41.3%	0.6%
Cytopenias				
Thrombocytopenia	61.3%	33.8%	5.6%	0.6%
Anemia	50.1%	25.3%	6.7%	0%
Neutropenia	30.2%	19.6%	6.1%	1.7%
Gastrointestinal				
Nausea	73.6%	3.0%	35.2%	1.1%
Constipation	39.8%	0.5%	20.1%	0.6%
Vomiting	34.3%	1.9%	16.2%	0.6%
Decreased appetite	25.3%	0.3%	14.5%	0.6%
Abdominal pain	22.6%	1.1%	29.6%	1.7%

14.7% discontinuation of niraparib due to AEs versus 2.2% in the placebo group

Mirza MR et al. *N Engl J Med* 2016; 375(22):2154-64

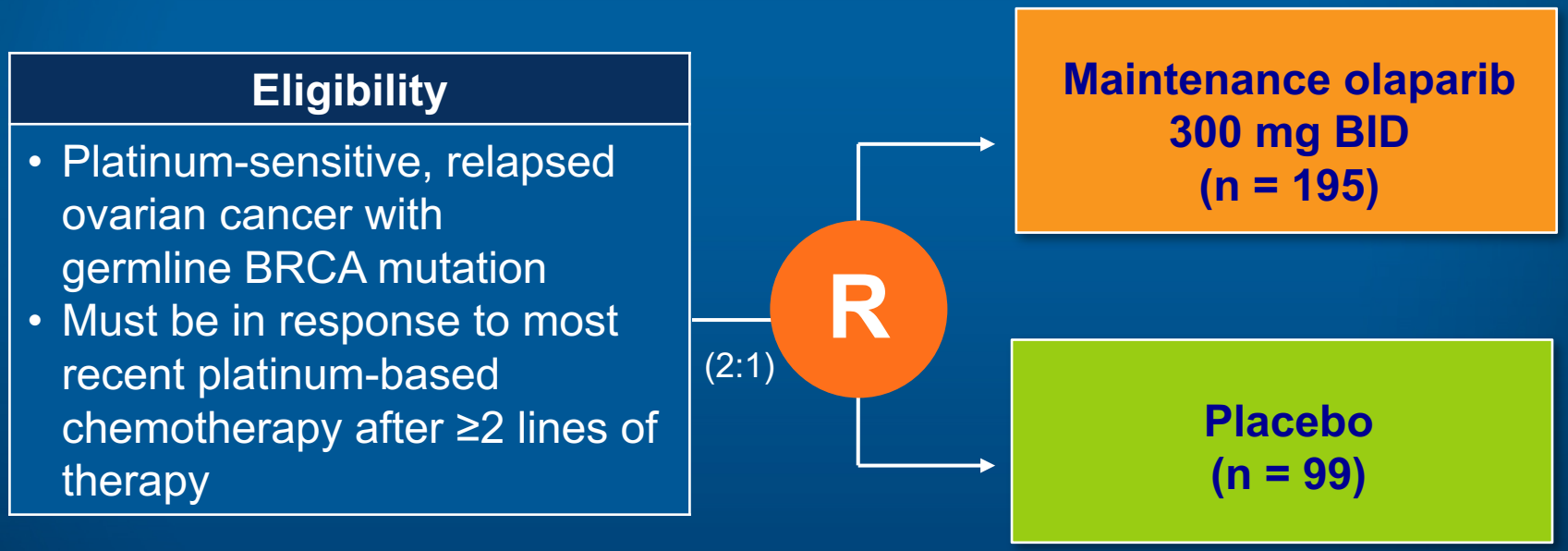
Press Release – March 27, 2017
FDA Approval of Niraparib as Maintenance Therapy

"The US Food and Drug Administration today approved niraparib for the maintenance treatment (intended to delay cancer growth) of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, whose tumors have completely or partially shrunk (complete or partial response, respectively) in response to platinum-based chemotherapy."

The approved administration of niraparib maintenance therapy is not dependent on the presence of a specific genetic mutation.

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm548948.htm

SOLO2 Phase III Trial of Olaparib Monotherapy as Maintenance



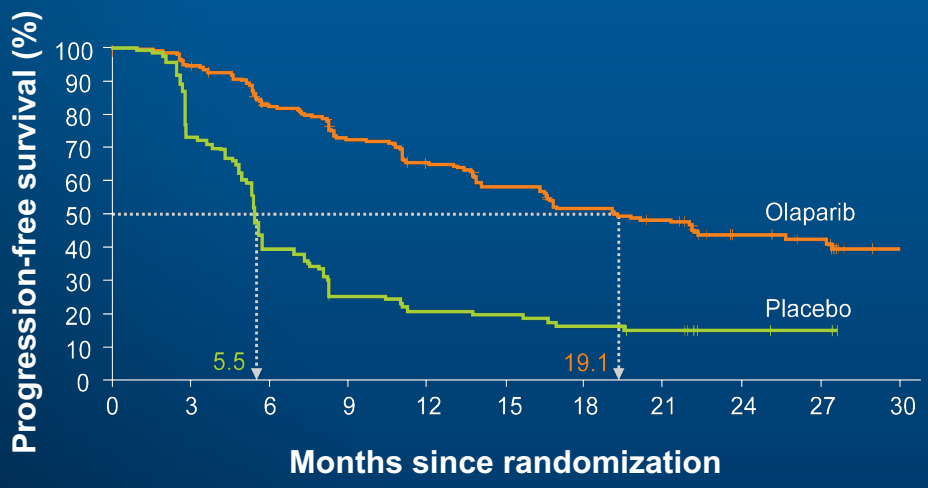
Primary endpoint: Investigator-assessed progression-free survival

Pujade-Lauraine E et al. *Proc SGO* 2017;Abstract LBA2.

SOLO2: PFS by Investigator and Blinded Independent Central Review (BICR)

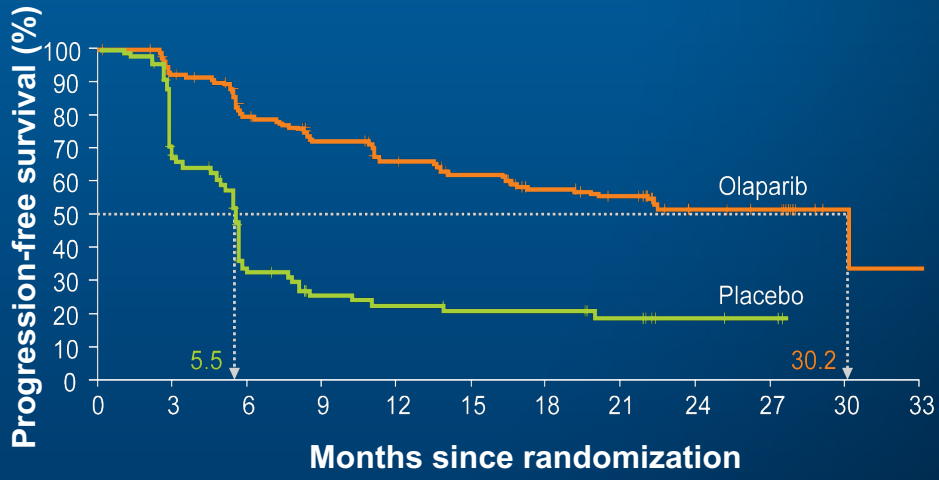
PFS by Investigator Assessment

Clinical endpoint	Olaparib (n = 196)	Placebo (n = 99)	HR (*p*-value)
Median PFS	19.1 mo	5.5 mo	0.30 (<0.0001)



PFS by BICR

Clinical endpoint	Olaparib (n = 196)	Placebo (n = 99)	HR (*p*-value)
Median PFS	30.2 mo	5.5 mo	0.25 (<0.0001)



Pujade-Lauraine E et al. *Proc SGO* 2017;Abstract LBA2.

Case 2 (Dr Liu)

- 74 year-old woman with high-grade serous ovarian cancer
- Prior treatment history:
  - Optimal cytoreductive surgery for stage III ovarian cancer; adjuvant chemotherapy with carboplatin/paclitaxel
  - Multiple subsequent lines of therapy
- No family history of breast, ovarian, endometrial, or colon cancer. Next-generation sequencing panel genetic testing without germline BRCA1/BRCA2 mutation; BARD1 VUS
- Tumor testing without somatic BRCA1/BRCA2 mutation

Case 2 (Dr Liu - Continued)

- Started on niraparib 300mg daily
- Side effects include fatigue and nausea
  - Nausea responds well to prochlorperazine taken slightly before niraparib dosing
- CBC trend during first 3 weeks of treatment:
  - Day 1: WBC 4.60, Hgb 10.1, Plt 275K
  - Day 15: WBC 3.79, Hgb 9.8, Plt 133K
  - Day 22: WBC 2.90, Hgb 8.8, Plt 15K
    - Niraparib held; platelet transfusion given
  - Day 24: WBC 3.0, Hgb 7.2, Plt 52K
    - PRBC transfusion given
  - Day 29: WBC 4.1, Hgb 9.1, Plt 159K
    - Niraparib resumed at 200mg daily
- CA125 decrease from 140 to 25 after 8 weeks of treatment
- Patient remains on treatment for 15 months before stopping for disease progression

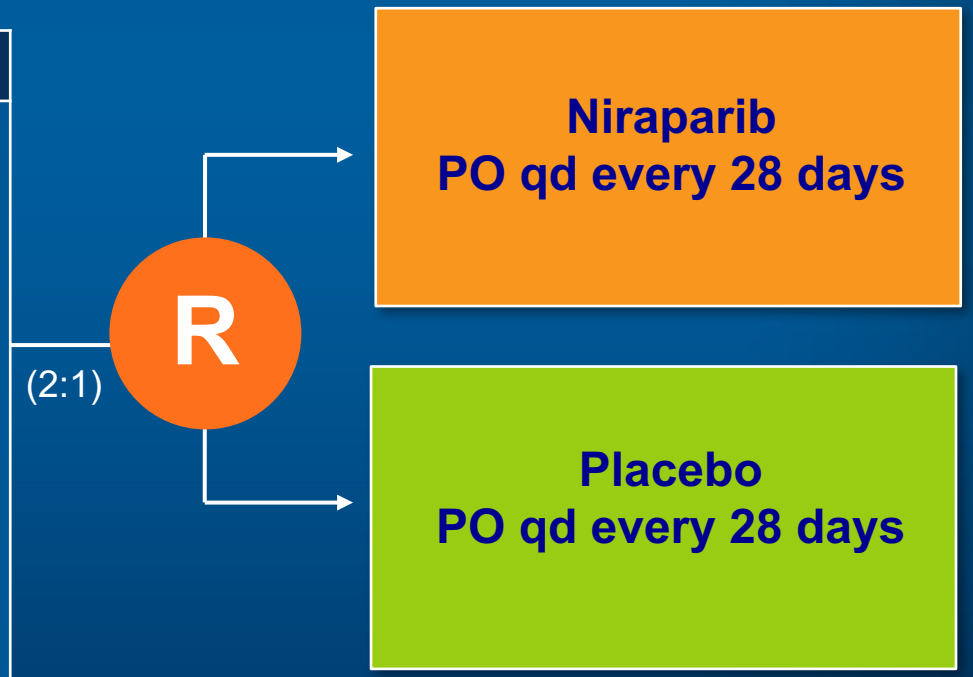
Novel Investigational Approaches

PRIMA Phase III Schema

Accrual: 330

Eligibility

- Stage III-IV ovarian, fallopian tube or peritoneal cancer
- Residual disease after debulking surgery, unless pt underwent neoadjuvant therapy
- Completed 4 cycles of platinum-based therapy, with a complete or partial response and CA-125 in the normal range or decreased by >90% during front-line therapy
- Must agree to undergo HRD testing



Primary endpoint: Progression-free survival

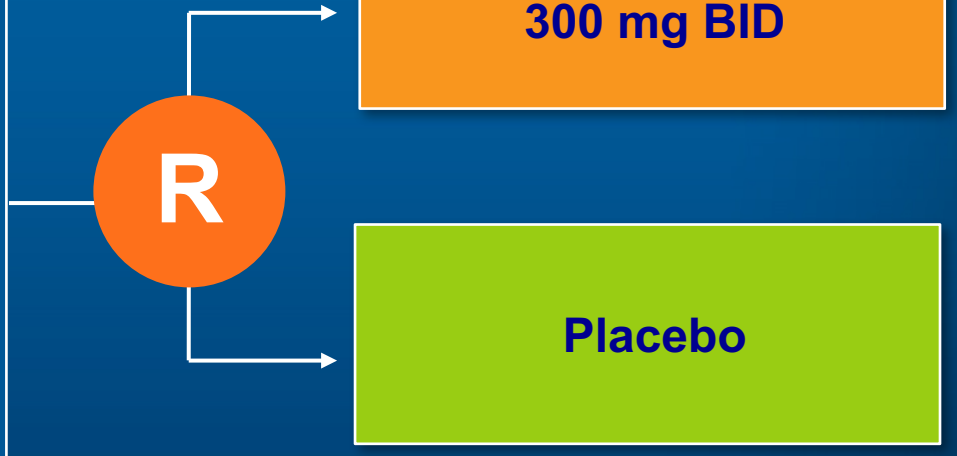
www.clinicaltrials.gov. Accessed June 2, 2017

SOLO-1 Phase III Trial of Olaparib Monotherapy as Maintenance

Target Accrual: 397

Eligibility

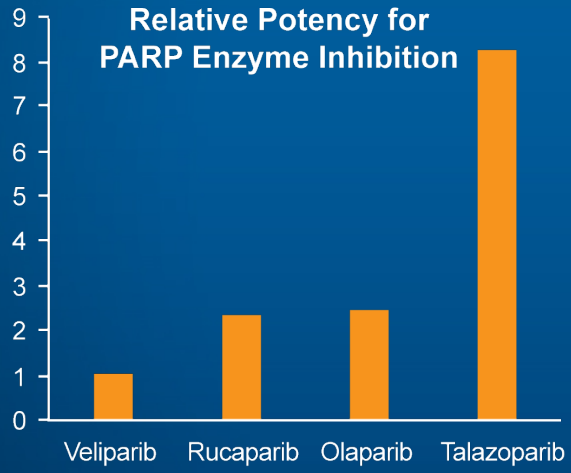
- Deleterious BRCA1 or BRCA2-mutant, high-grade serous or endometrioid ovarian, primary peritoneal and/or fallopian tube cancer
- Completed first-line platinum-based chemotherapy
- CR or PR after completion of first-line chemotherapy

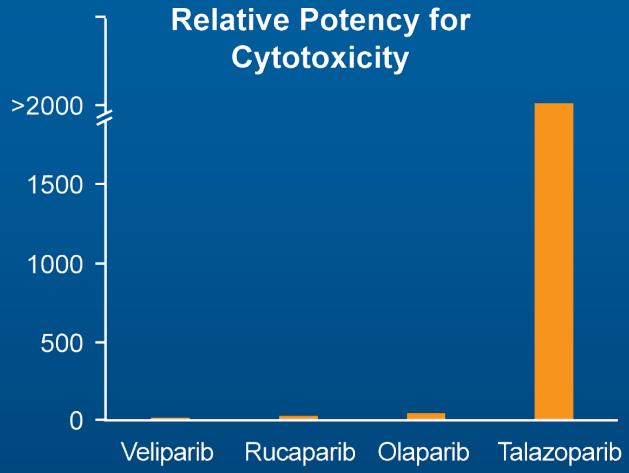


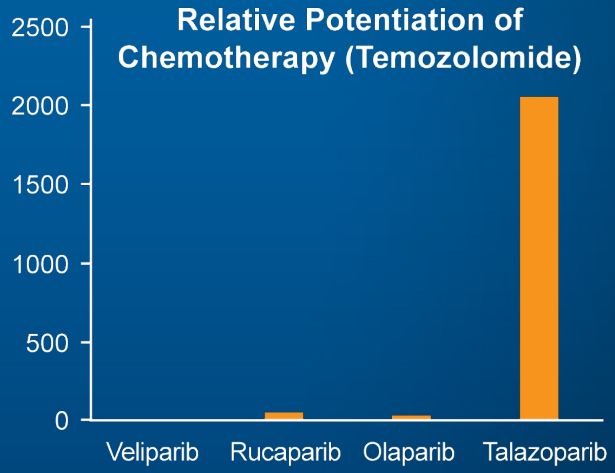
Primary endpoint: Progression-free survival

www.clinicaltrials.gov. Accessed June 2, 2017 (NCT01844986)

Potency and PARP Trapping of PARP Inhibitors







Shen Y et al. *Clin Cancer Res* 2013;19:5003-15.

PARP Trapping Potency

PARP inhibitor	Catalytic inhibition (IC50 nM)	Cytotoxicity (IC90 uM)	PARP-trapping potency (relative to olaparib set at 1)
Veliparib	30	>50	<0.2
Olaparib	6	4.5	1
Rucaparib	21	3	1
Niraparib	60	2.3	~2
Talazoparib	4	0.04	~100

Pommier Y. International Congress on Targeted Anticancer Therapies 2015

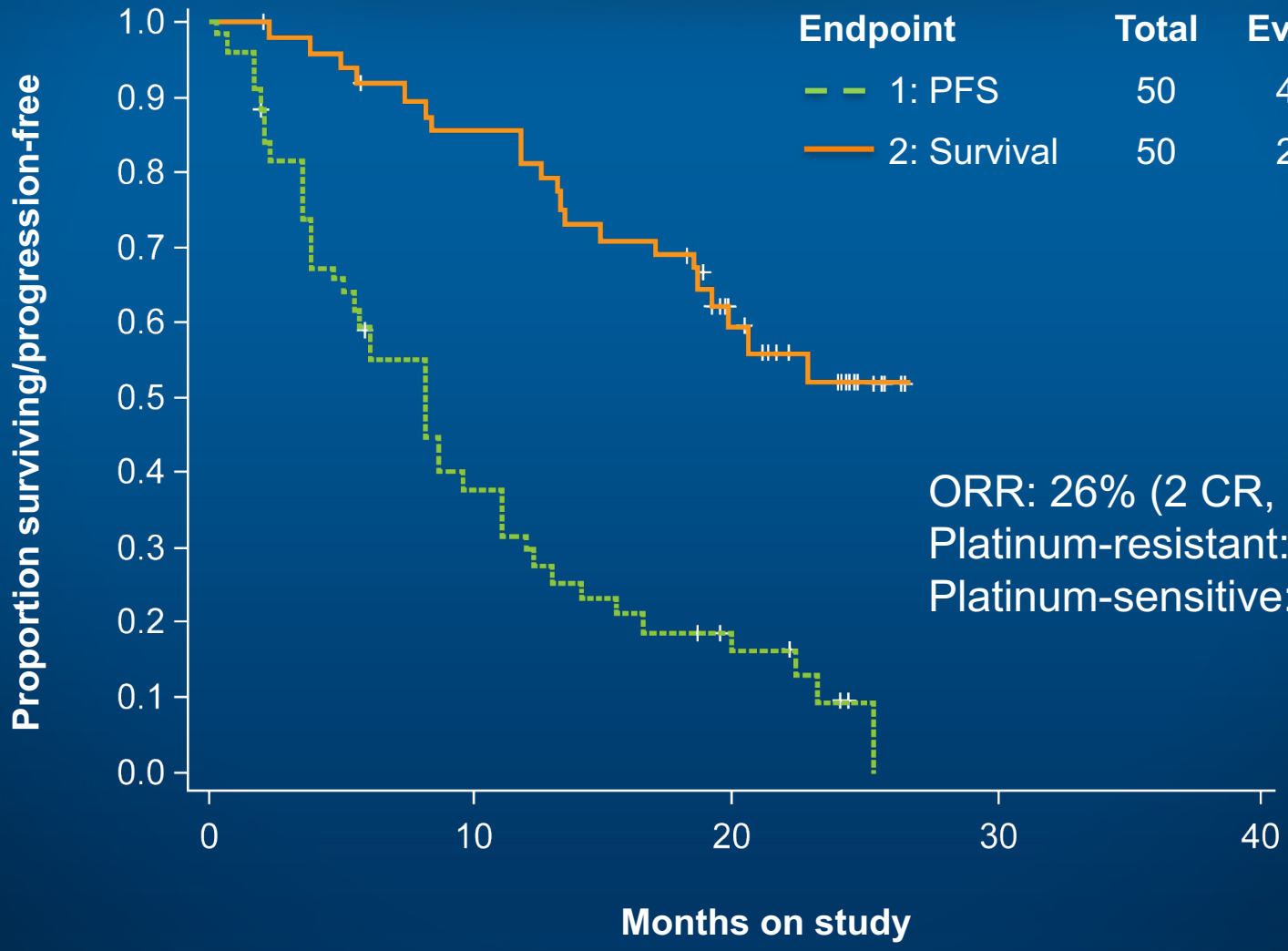
Gynecol Oncol. 2015 June ; 137(3): 386–391. doi:10.1016/j.ygyno.2015.03.042.

A phase II evaluation of the potent, highly selective PARP inhibitor veliparib in the treatment of persistent or recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in patients who carry a germline BRCA1 or BRCA2 mutation – an NRG Oncology/Gynecologic Oncology Group study

Robert L. Coleman, MD[1,*], **Michael W. Sill, PhD**[2], **Katherine Bell-McGuinn, MD**[3], **Carol Aghajanian, MD**[3], **Heidi J. Gray, MD**[4], **Krishnansu S. Tewari, MD**[5], **Steven C. Rubin, MD**[6], **Thomas J. Rutherford, MD**[7], **John K Chan, MD**[8], **Alice Chen**[9], and **Elizabeth M. Swisher, MD**[10]

[1]Dept. of Gynecologic Oncology & Reproductive Medicine, University of Texas, M.D. Anderson Cancer Center, Houston, TX 77030

Veliparib in BRCA-Mutant Ovarian Cancer: Survival and Response Analyses



Colemen RL et al. *Gynecol Oncol* 2015;137(3):386-91.

Veliparib: Select Adverse Events

	N = 50	
Event	**Any grade**	**Grade 3/4**
Fatigue	32%	6%
Cytopenias		
Thrombocytopenia	18%	2%
Anemia	48%	0%
Neutropenia	30%	2%
Gastrointestinal		
Nausea	86%	4%
Vomiting	58%	0%
Other gastrointestinal	66%	0%

11/50 (22%) patients discontinued treatment due to toxicity

Colemen RL et al. *Gynecol Oncol* 2015;137(3):386-91.

A Phase I Study of Continuous Veliparib in Combination with IV Carboplatin/Paclitaxel or IV/IP Paclitaxel/Cisplatin and Bevacizumab in Newly Diagnosed Patients with Previously Untreated Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer: An NRG Oncology/Gynecologic Oncology Group Study

Bell-McGuinn KM et al.
Proc ASCO 2015;Abstract 5507.

Study Schema

Previously untreated epithelial ovarian, fallopian tube or primary peritoneal carcinoma or carcinosarcoma
Stage II-IV
(n = 189)

Regimen I (n = 80)
Paclitaxel 175 mg/m^2 IV, Day 1
Carboplatin AUC 6 IV, Day 1

Regimen II (n = 48)
Paclitaxel 80 mg/m^2 IV, Day 1, 8, 15
Carboplatin AUC 6 IV, Day 1

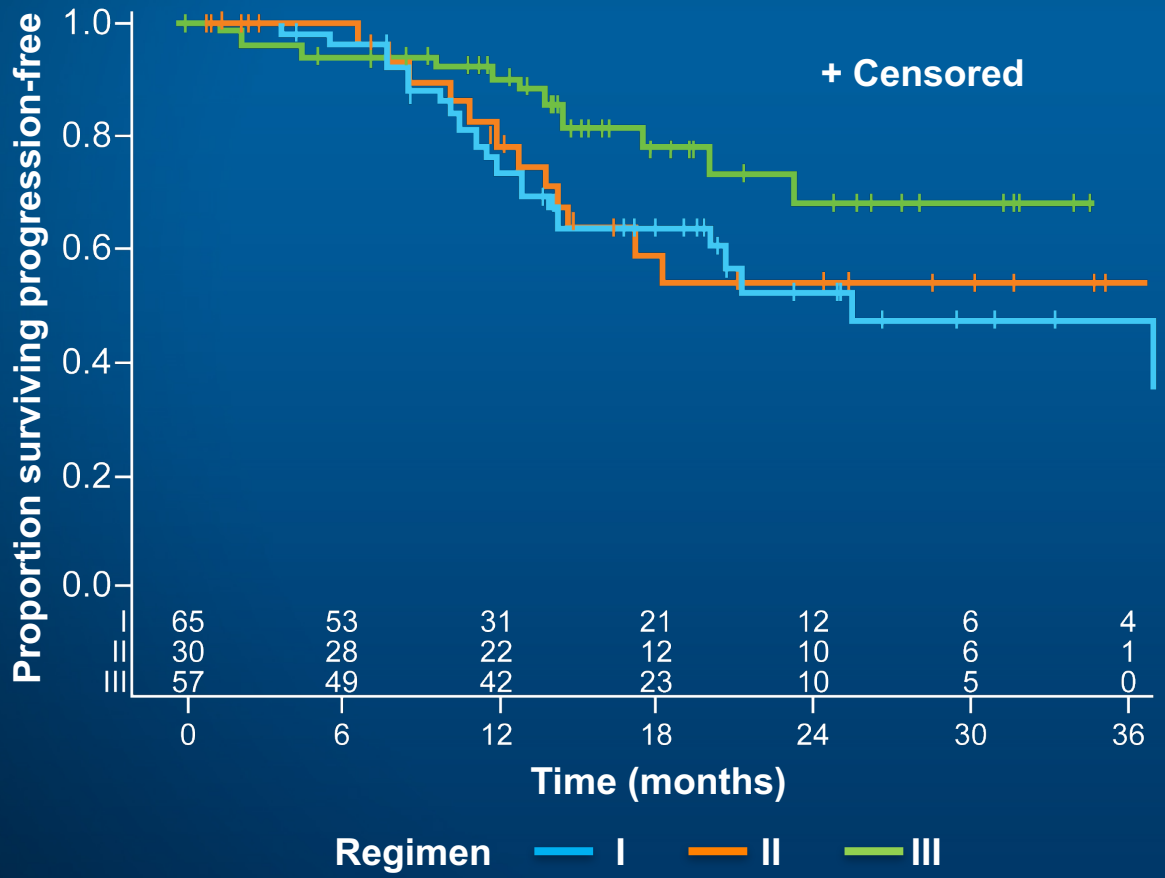
Regimen III (n = 57)
Paclitaxel 135 mg/m^2 IV, Day 1
Cisplatin 75 mg/m^2 IP, Day 1 or 2
Paclitaxel 60 mg/m^2 IP, Day 8

Veliparib dose levels
30 mg
50 mg
80 mg
100 mg
150 mg
200 mg
250 mg
300 mg

Veliparib twice daily PO, Days 1-21, cycles 1-6
Bevacizumab 15 mg/kg IV, Day 1, cycles 2-22

Bell-McGuinn KM et al. *Proc ASCO* 2015;Abstract 5507.

Progression Free Survival for Dose Levels of Veliparib ≥ 100mg BID



Regimen	Median PFS months
I	25
II	Not yet reached
III	Not yet reached

Regimen	PFS at 24 months
I	53%
II	54%
III	68%

Bell-McGuinn KM et al. *Proc ASCO* 2015;Abstract 5507.

Phase III Study of Chemotherapy with and without Concurrent and Continuation Maintenance Veliparib

Target Accrual: 1,100

Eligibility

- Stage III-IV epithelial ovarian, fallopian tube or peritoneal cancer
- High-grade serous adenocarcinoma
- Willing to undergo testing for gBRCA
- Archived diagnostic FFPE tumor tissue, or tumor tissue biopsy collected prior to C1D1

Carboplatin/paclitaxel + placebo → placebo maintenance

Carboplatin/paclitaxel + veliparib → placebo maintenance

Carboplatin/paclitaxel + veliparib → veliparib maintenance

Primary endpoint: Progression-free survival

www.clinicaltrials.gov. Accessed June 2, 2017 (NCT02470585)

Phase I Study of Talazoparib in BRCA-Mutant OC (Median Prior Chemo Regimens: 3)

Genetic status	N	RECIST Response			
		PR/CR		SD ≥ 24 wks	SD ≤ 24 wks or PD
		RECIST*	CA-125†		
Deleterious BRCA1m	20	8	13	4	3
Deleterious BRCA2m	8	4	6	0	2
Total	28	12 (48%)	19 (70%)	4 (14%)	5 (18%)

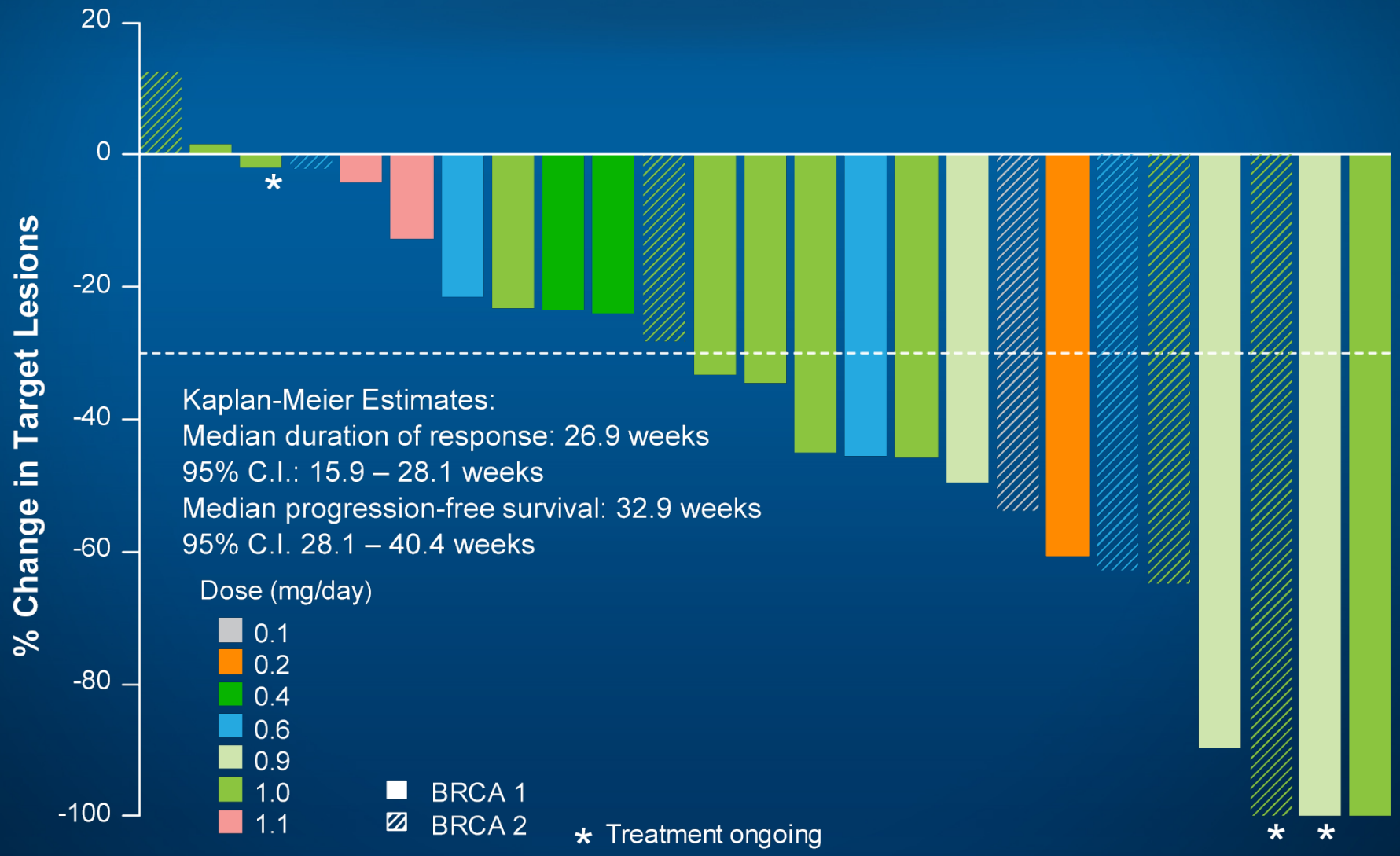
25/28 patients evaluable by RECIST; † 27/28 patients evaluable for CA-125

RECIST response:

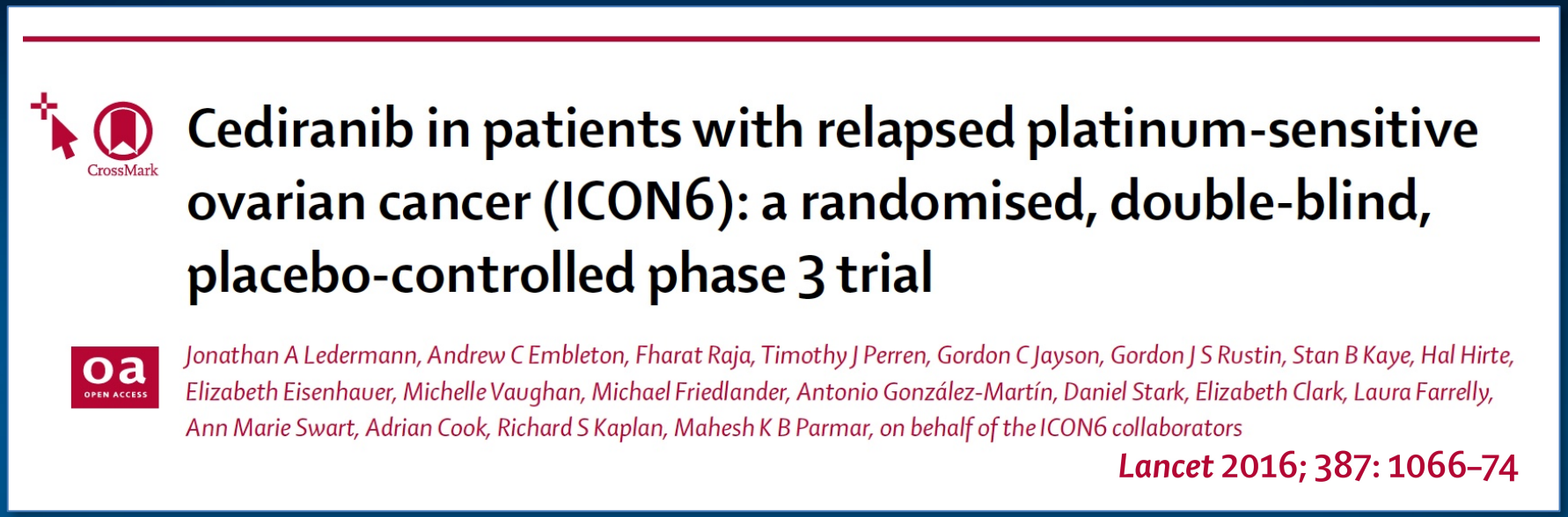
- ORR: 12/25 (48%)
- CBR ≥24 weeks: 23/28 (82%)

Wainberg ZA et al. *Proc ASCO* 2014;Abstract 7522.

Best Response of Talazoparib



Wainberg ZA et al. *Proc ASCO* 2014;Abstract 7522.



Cediranib in patients with relapsed platinum-sensitive ovarian cancer (ICON6): a randomised, double-blind, placebo-controlled phase 3 trial

Jonathan A Ledermann, Andrew C Embleton, Fharat Raja, Timothy J Perren, Gordon C Jayson, Gordon J S Rustin, Stan B Kaye, Hal Hirte, Elizabeth Eisenhauer, Michelle Vaughan, Michael Friedlander, Antonio González-Martín, Daniel Stark, Elizabeth Clark, Laura Farrelly, Ann Marie Swart, Adrian Cook, Richard S Kaplan, Mahesh K B Parmar, on behalf of the ICON6 collaborators

Lancet 2016; 387: 1066–74

Overall Survival Results of ICON6: A Trial of Chemotherapy and Cediranib in Relapsed Ovarian Cancer

Ledermann JA et al.
Proc ASCO 2017;Abstract 5506.

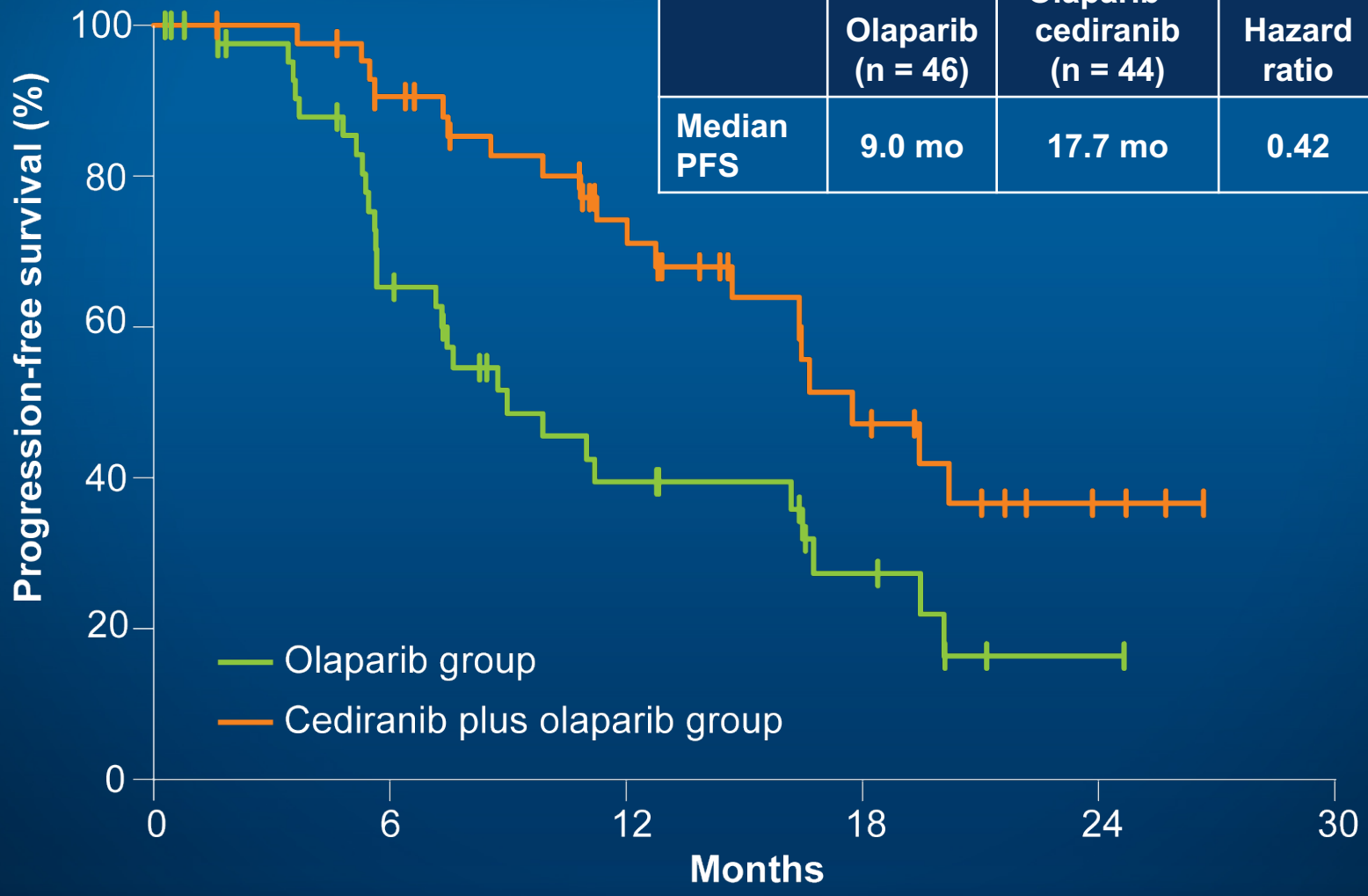
Combination cediranib and olaparib versus olaparib alone for women with recurrent platinum-sensitive ovarian cancer: a randomised phase 2 study

Joyce F Liu, William T Barry, Michael Birrer, Jung-Min Lee, Ronald J Buckanovich, Gini F Fleming, BJ Rimel, Mary K Buss, Sreenivasa Nattam, Jean Hurteau, Weixiu Luo, Philippa Quy, Christin Whalen, Lisa Obermayer, Hang Lee, Eric P Winer, Elise C Kohn, S Percy Ivy, Ursula A Matulonis

Lancet Oncol 2014; 15: 1207–14

Progression-Free Survival: Olaparib/Cediranib

	Olaparib (n = 46)	Olaparib + cediranib (n = 44)	Hazard ratio	*p*-value
Median PFS	9.0 mo	17.7 mo	0.42	0.005



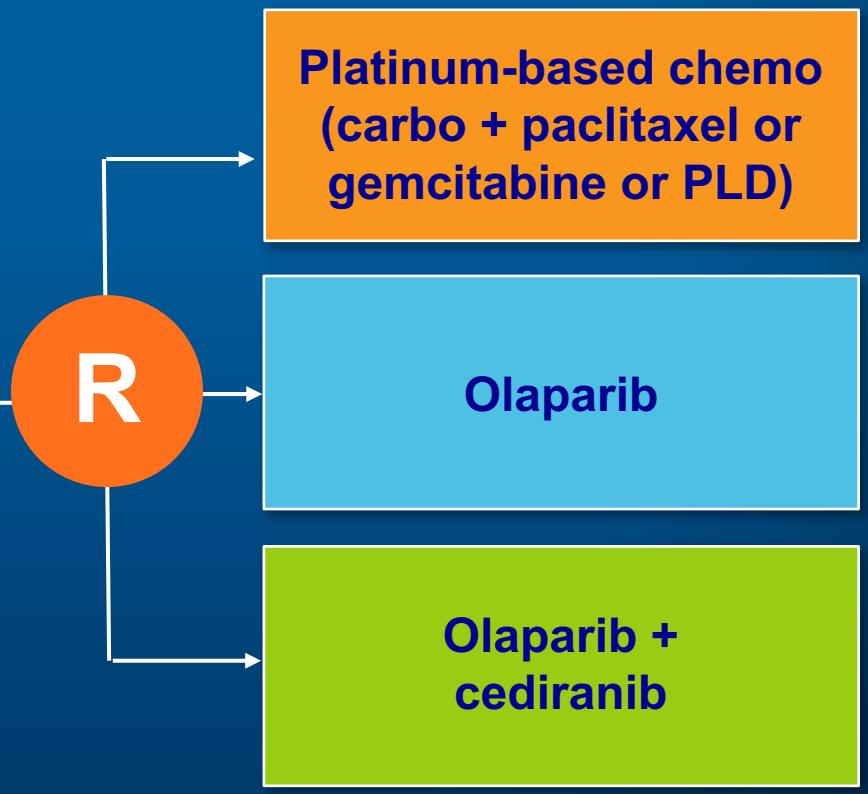
Liu JF et al. *Lancet Oncol* 2014;15:1207-14.

NRG-GY004 Phase III Study Schema

Target Accrual: 450

Eligibility

- Platinum-sensitive recurrent high-grade serous or high-grade EOC, primary peritoneal or fallopian tube cancers
- No prior anti-angioenic or PARP inhibitor treatments



Primary endpoint: Progression-free survival

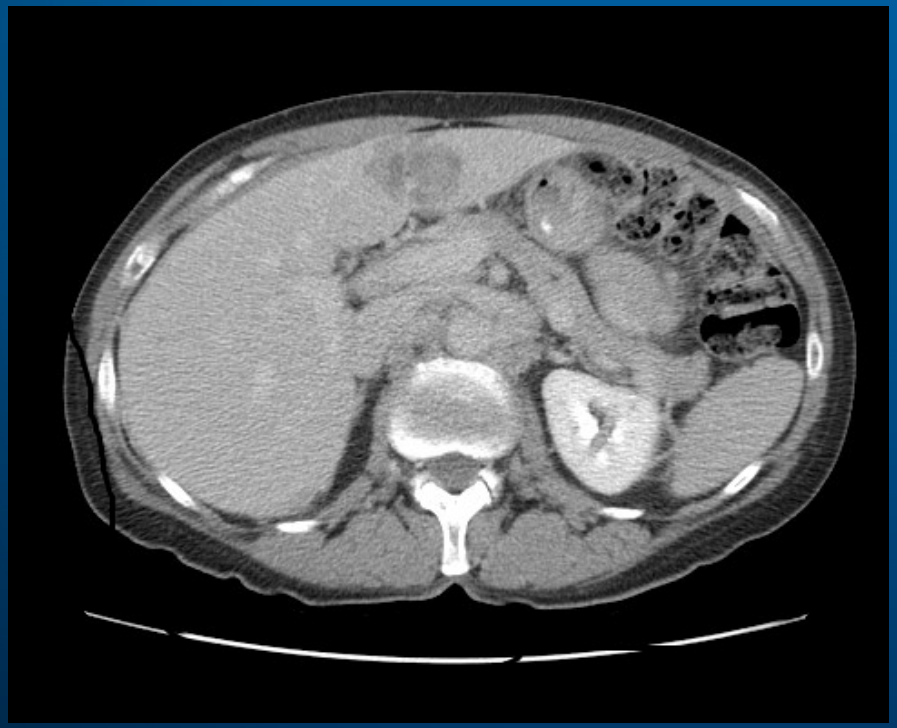
www.clinicaltrials.gov. Accessed June 2, 2017 (NCT02446600)

Case 3 (Dr Birrer)

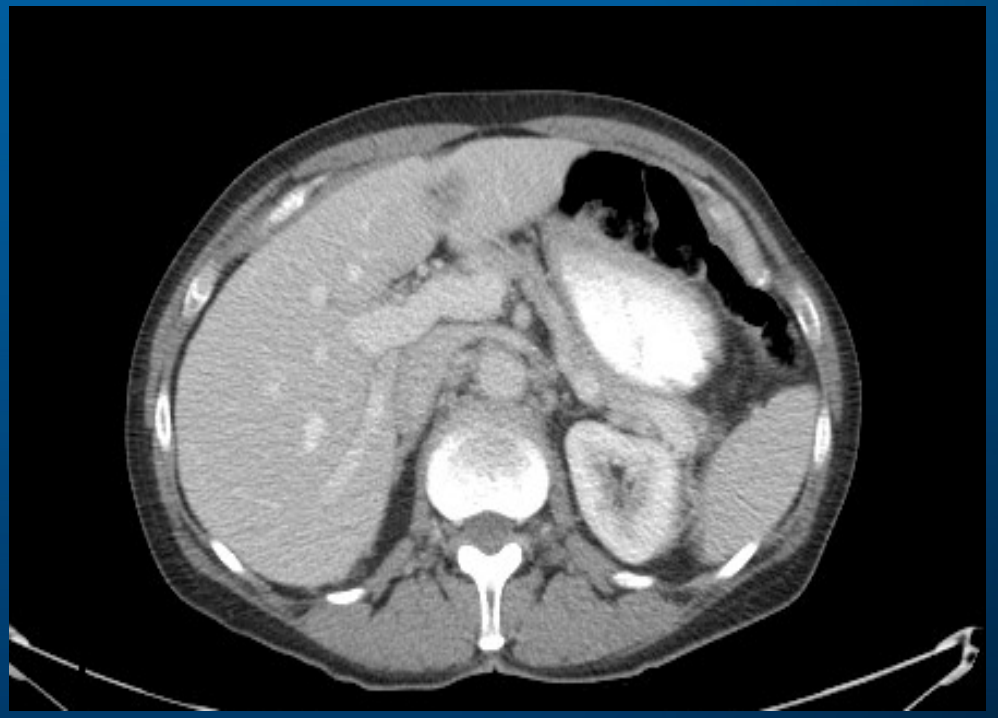
- A 70-yo woman diagnosed in 8/13 with high grade serous cancer of the ovary
- She was treated with neoadjuvant carbo/paclitaxel
- Optimal cytoreduction in 11/13 followed by 3 cycles of carbo/paclitaxel (2/14)
- Recurrent disease in 8/14 started on early phase trial CRLX101 + bevacizumab
- Progressive disease 9/15
- Started on Phase I trial of mirvetuximab soravtansine

Case 3 (Dr Birrer - Continued)

Initial Scan



After 2 cycles

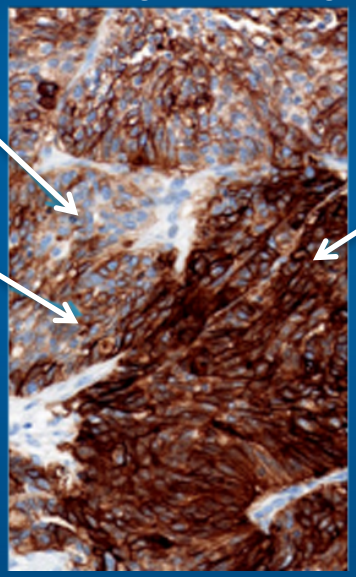


Case 3 (Dr Birrer - Continued)

- Stayed on trial for 19 cycles
- PD on 2/1/17
- Minimal toxicity—only grade 1 dry eyes

Folate Receptor Alpha Expression Distribution

Staining & Scoring



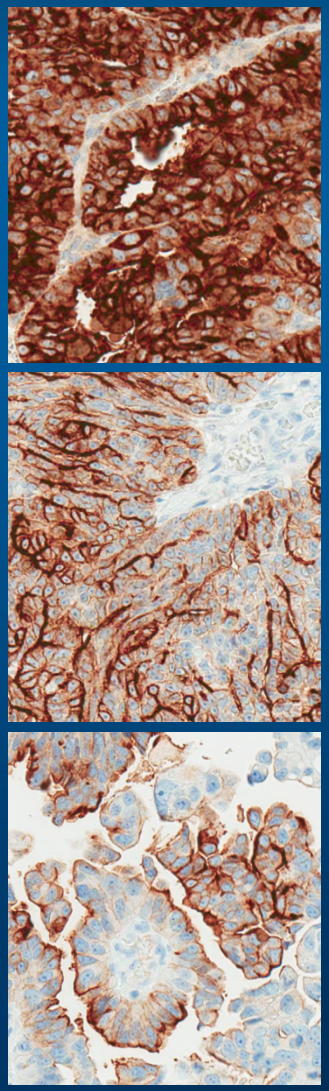
Low 18%*
(25-49 ≥2+)

High 50%
(≥75 ≥2+)

Medium 32%
(50-74 ≥2+)

Membrane staining	Intensity score	Percentage of cells (%)
Strong	3	60
Moderate	2	25
Weak	1	10
Negative	0	5

hscore = 240/high expression



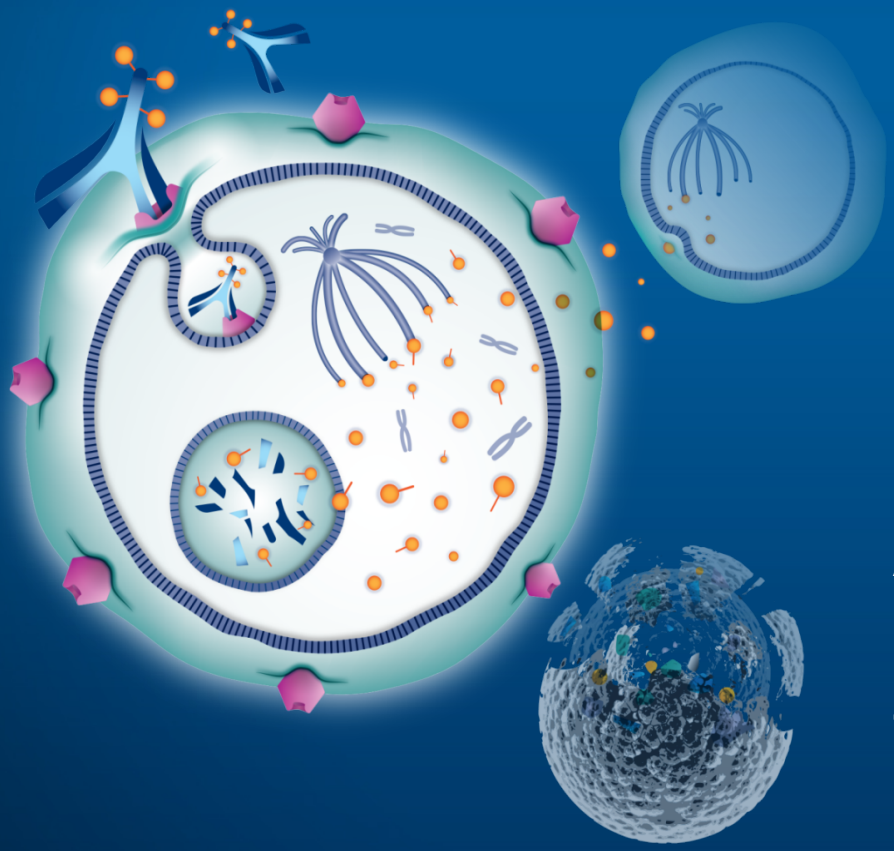
High

Medium

Low

Courtesy of Michael J Birrer, MD, PhD

Mirvetuximab Soravtansine (IMGN853) Mechanism of Action



AN INTEGRATED SYSTEM

Linker

- Cleavable linker stable in the blood stream
- Bystander killing of neighboring cancer cells

Ultra-potent anticancer agent

- DM4 — a potent tubulin-targeting agent

Antibody (Ab)

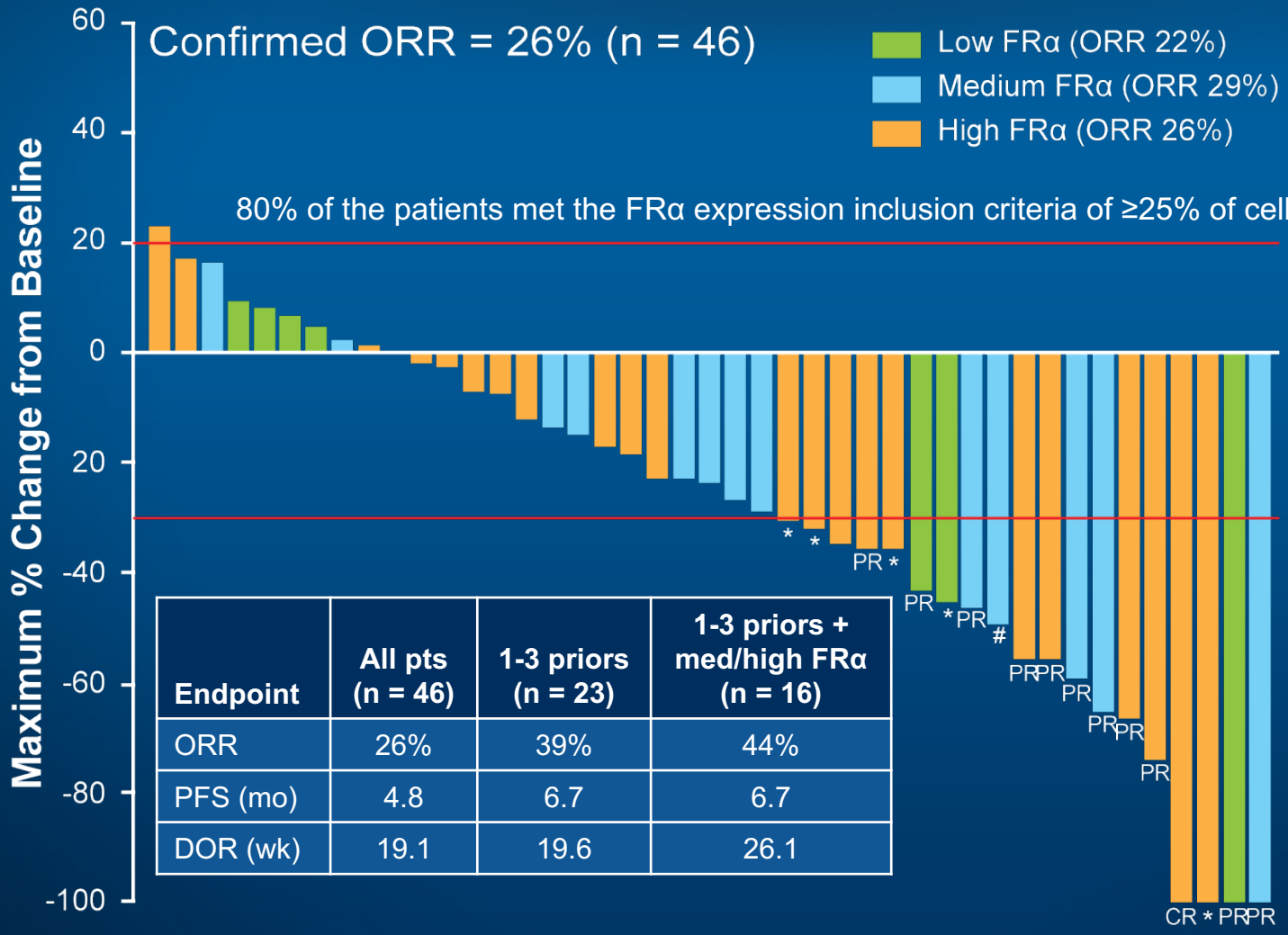
- A folate receptor α (FRα)-binding antibody

Target

- Highly expressed in ovarian and other cancers

Martin LP et al. AACR/EORTC/NCI 2015;Poster C47.

Mirvetuximab Soravtansine Monotherapy in Platinum-Resistant EOC

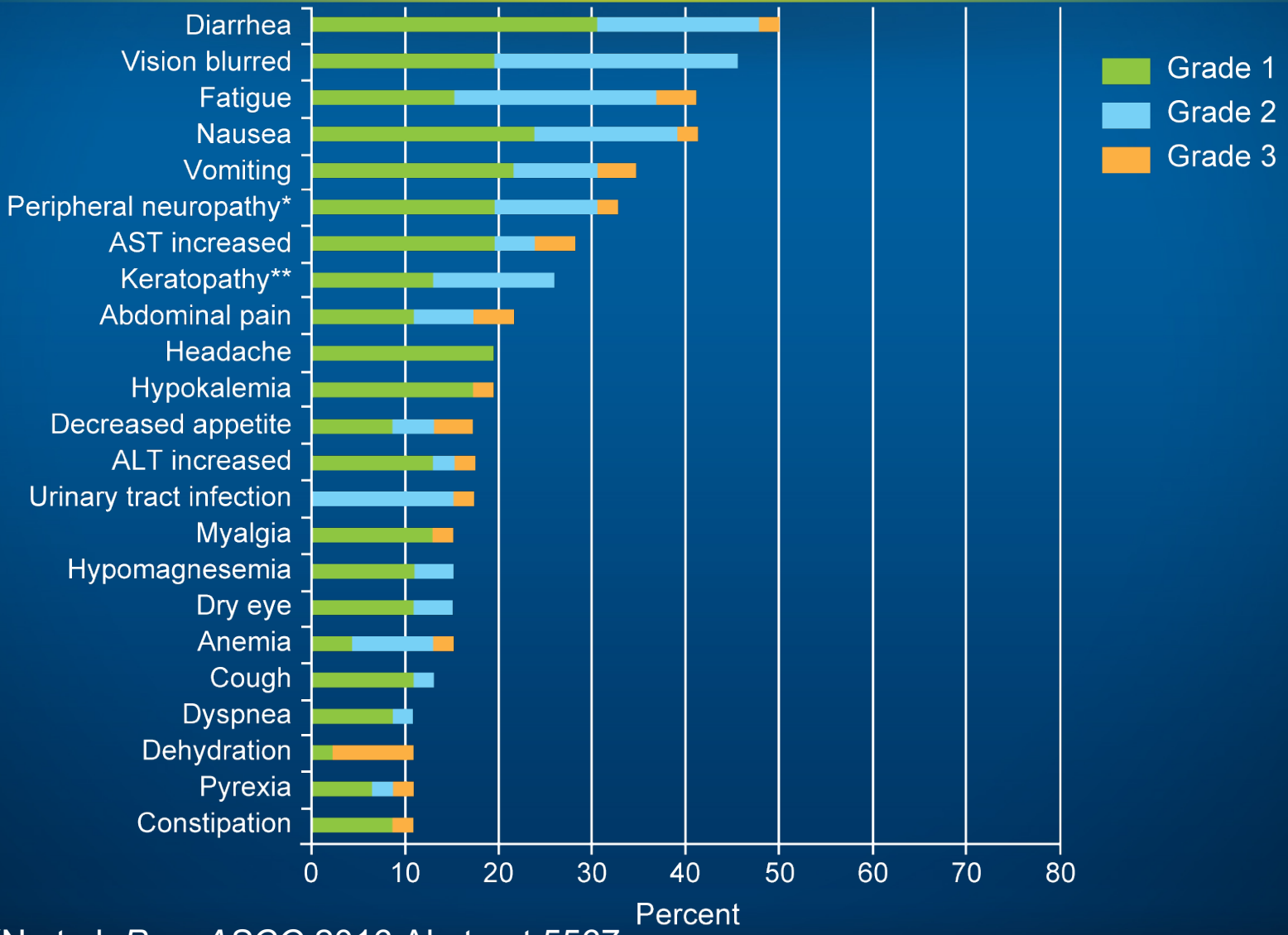


Endpoint	All pts (n = 46)	1-3 priors (n = 23)	1-3 priors + med/high FRα (n = 16)
ORR	26%	39%	44%
PFS (mo)	4.8	6.7	6.7
DOR (wk)	19.1	19.6	26.1

CR, Complete Response
PR, Partial Response
*, Unconfirmed PR
#, Mixed Response

Moore KN et al. *Proc ASCO* 2016;Abstract 5567.

Mirvetuximab Soravtansine-Associated AEs in >10% of Patients (N = 46)



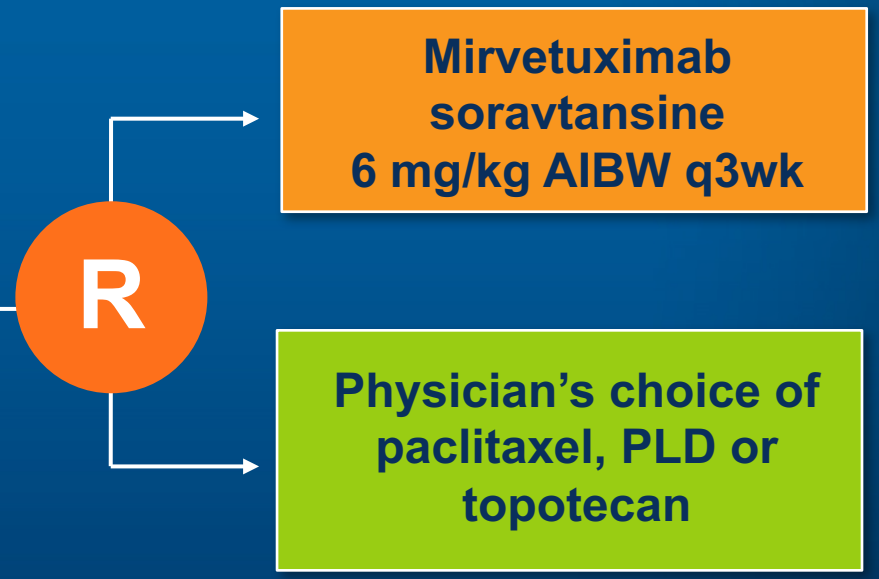
Moore KN et al. *Proc ASCO* 2016;Abstract 5567.

FORWARD I: A Phase III Study of Mirvetuximab Soravtansine

Trial Identifier: NCT02631876
Enrollment: 333 (Open)

Eligibility

- Advanced EOC, primary peritoneal or fallopian tube cancer
- Folate receptor alpha-positive
- Platinum resistant
- At least 1 but no more than 3 prior systemic treatment regimens



Primary endpoint: Progression-free survival in all patients and those with high folate receptor expression

www.clinicaltrials.gov. Accessed June 2017.

VOLUME 33 · NUMBER 34 · DECEMBER 1 2015

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Safety and Antitumor Activity of Anti–PD-1 Antibody, Nivolumab, in Patients With Platinum-Resistant Ovarian Cancer

Junzo Hamanishi, Masaki Mandai, Takafumi Ikeda, Manabu Minami, Atsushi Kawaguchi, Toshinori Murayama, Masashi Kanai, Yukiko Mori, Shigemi Matsumoto, Shunsuke Chikuma, Noriomi Matsumura, Kaoru Abiko, Tsukasa Baba, Ken Yamaguchi, Akihiko Ueda, Yuko Hosoe, Satoshi Morita, Masayuki Yokode, Akira Shimizu, Tasuku Honjo, and Ikuo Konishi

Efficacy of Nivolumab in Platinum-Resistant Ovarian Cancer

PD-1 inhibitor	No. pts	ORR	DCR	Median PFS	Median OS
Nivolumab 1 & 3 mg/kg	20	3/20 (15%)	9/20 (45%)	3.5 mo	20.0 mo

Grade 3/4 AE rate: 8/20 (40%)

Hamanishi J et al. *J Clin Oncol* 2015;33(34):4015-22.

Ongoing Investigations of Anti-PD-1/PD-L1 Checkpoint Inhibitors in Ovarian Cancer

- 31 ongoing studies specific to ovarian, fallopian tube and peritoneal cancers
- Anti-PD-1/PD-L1 antibodies: Atezolizumab, avelumab, durvalumab, nivolumab, pembrolizumab
- Most studies in the platinum-resistant, recurrent setting
- Most studies in combination with bevacizumab, chemotherapy ± bevacizumab, targeted therapy or other immunotherapy
- Several front-line studies in combination with chemotherapy
- 5 Phase III studies identified
  - ATALANTE: Atezolizumab + platinum-containing chemo + bev in late relapse
  - NCI-2016-01081: PLD/atezolizumab ± bevacizumab vs PLD/bevacizumab in platinum-resistant, relapsed
  - JAVELIN Ovarian 200: Avelumab, PLD or the combination in platinum relapsed
  - IMagyn050: Carbo/paclitaxel/bev ± atezolizumab in newly diagnosed Stage III-IV
  - JAVELIN Ovarian 100: Chemo ± avelumab maintenance, chemo + avelumab followed by avelumab maintenance

www.clinicaltrials.gov. Accessed Feb 27, 2017.

Breakfast with the Investigators:
New Agents and Strategies in the Management of Ovarian Cancer

Sunday, June 4, 2017
6:45 AM – 7:45 AM
Chicago, Illinois

Faculty

Michael Birrer, MD, PhD
Joyce F Liu, MD, MPH
Mansoor Raza Mirza, MD

Moderator

Neil Love, MD

Research To Practice®

Please complete your CME Evaluation and turn it in to our staff as you exit the activity