# PARP inhibitors current applications and future prospects

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# Outline

- Background to the development of PARP inhibitors in ovarian cancer
- Maintenance Strategies in recurrent ovarian cancer
- Single agent therapy with PARP inhibitors
- Combination strategies- ’2nd generation studies’
- Horizon- how research might initiatives affect practice?

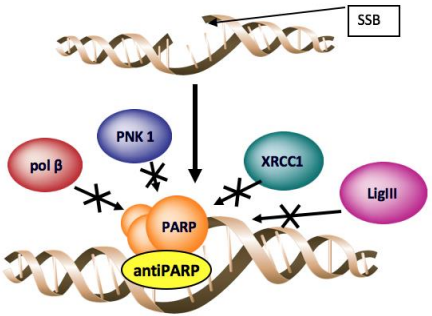
# Current treatment: Platinum combinations for recurrent ovarian cancer

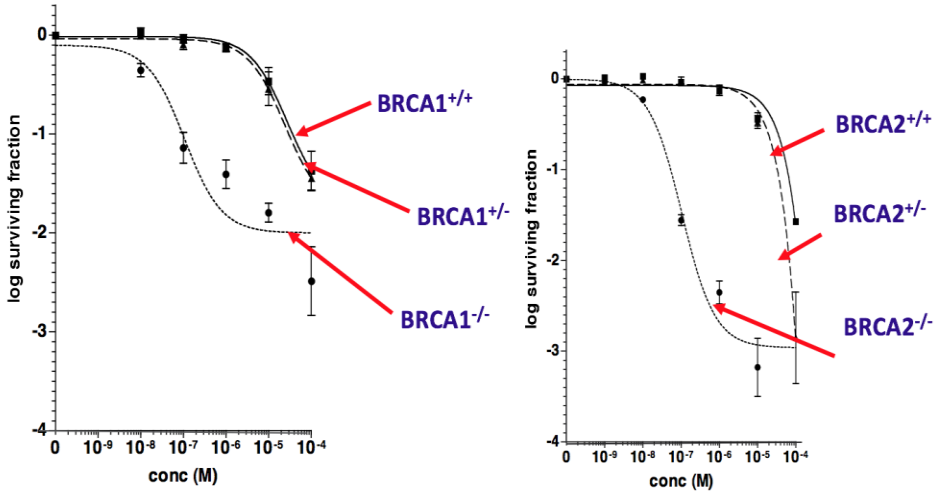
| Trial | Regimen | Med PFS |
|---|---|---|
| ICON 4 | Carboplatin/Paclitaxel | 12.0 |
| CALYPSO | Carboplatin /Paclitaxel | 9.4 |
| CALYPSO | Carboplatin/ PLD | 11.3 |
| OVAR 2.5 | Carboplatin/Gemcitabine | 8.6 |
| OCEANS (control) | Carboplatin/Gemcitabine | 7.4 |


- Gaps between successive lines of treatment become shorter
- Targeted - personalised treatment with markers predictive of a response are needed
- New treatments needed to extend chemotherapy-free periods and maintain QoL

# PARP INHIBITORS

## Poly(ADP-ribose) polymerase and DNA Repair



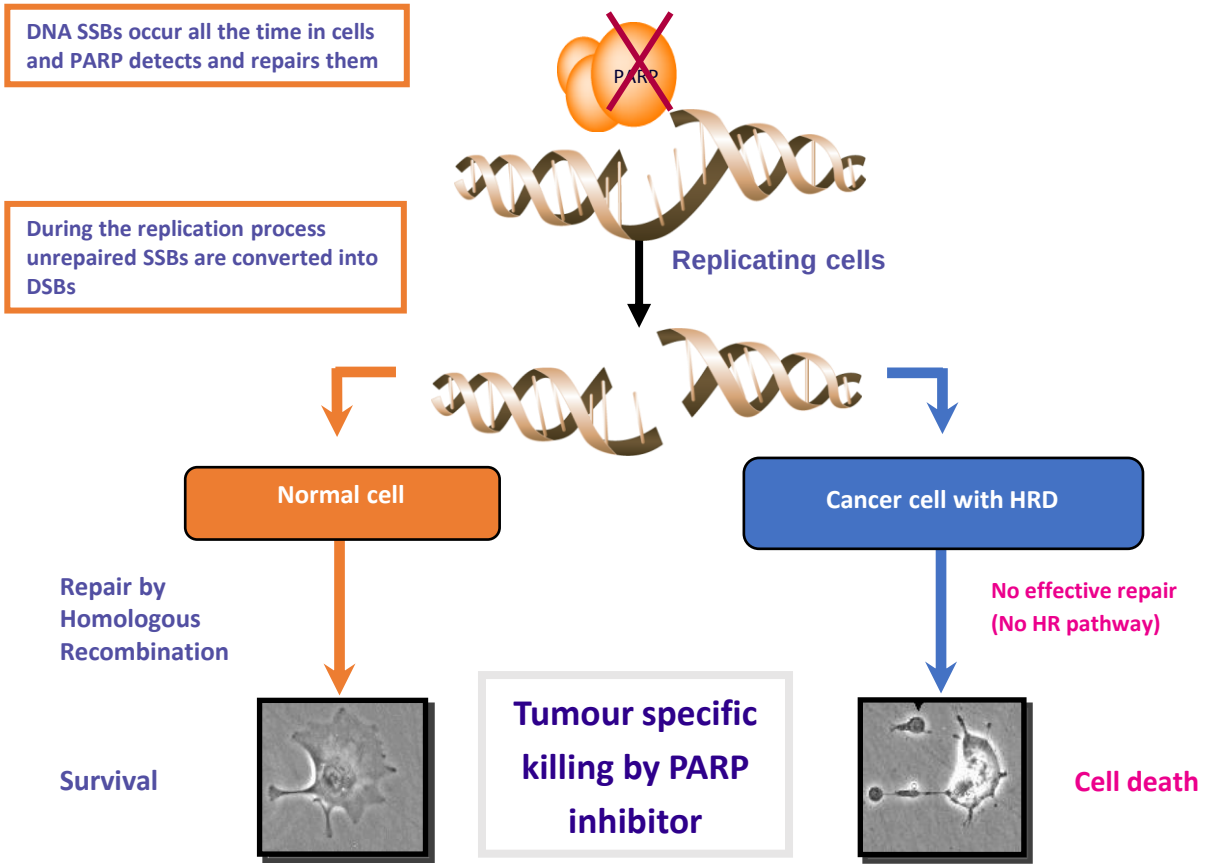




Farmer et al Nature 2005

- PARP is a key regulator of DNA damage repair processes
- Involved in DNA base-excision repair (BER)
- Binds directly to DNA damage
- Produces large branched chains of poly(ADP-ribose)
- Attracts and assists BER repair effectors

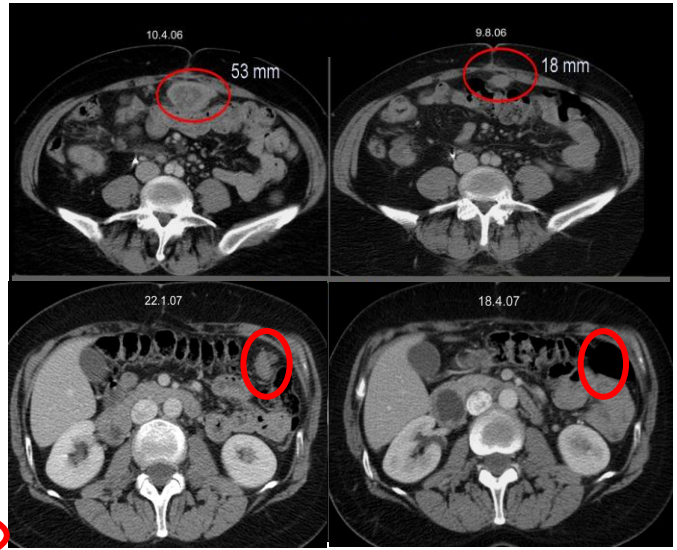
DNA Repair Defect
Homologous Recombination Deficiency

# PARP Inhibitors and Homologous Recombination repair of DNA damage



# Olaparib : an orally active PARP inhibitor

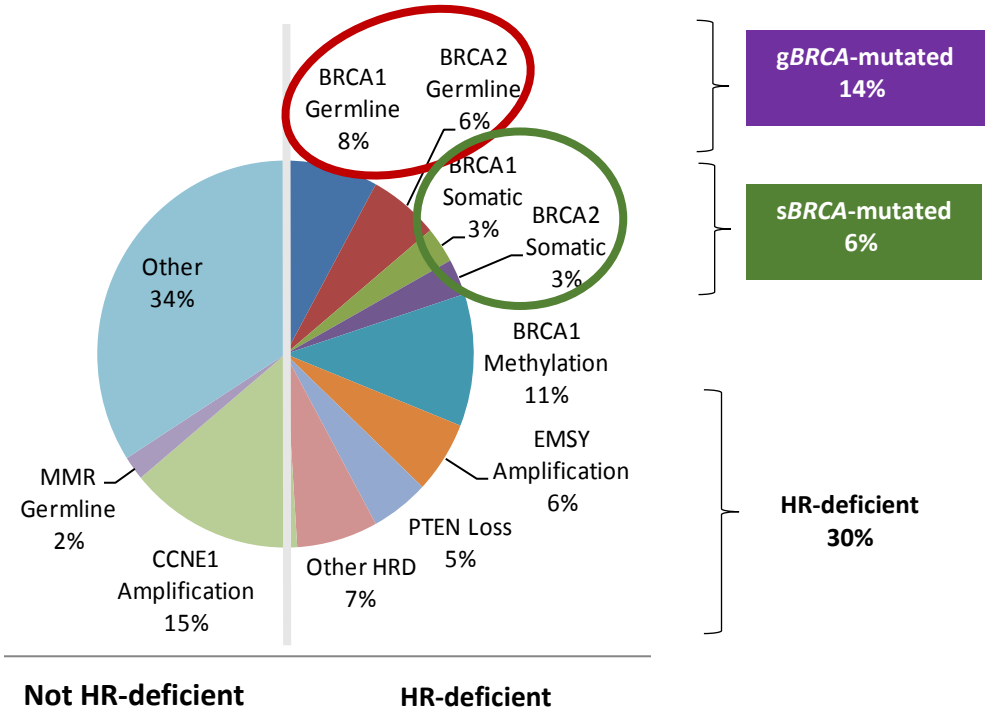
| | Olaparib Phase I and *BRCA* mutation expansion studies[1,2] | Olaparib multicentre Phase II *BRCA* mutation ovarian cancer study[3] |
|---|---|---|
| **Olaparib dose** | 200 mg bid | 400 mg bid |
| **RECIST CR/PR** | 14/50 (28%) | 11/33 (33%) |
| **SD ≥4 months** | 3/50 (6%) | 12/33 (36%) |
| **Overall** | 17/50 (34%) | 23/33 (69%) |
| **Median duration of response** | 7.0 months | 9.5 months |




PR: partial response, SD: stable disease

1.Fong et al., N Engl J Med 2009;
2. Fong et al., J Clin Oncol 2010;
3. Audeh et al. Lancet 2010

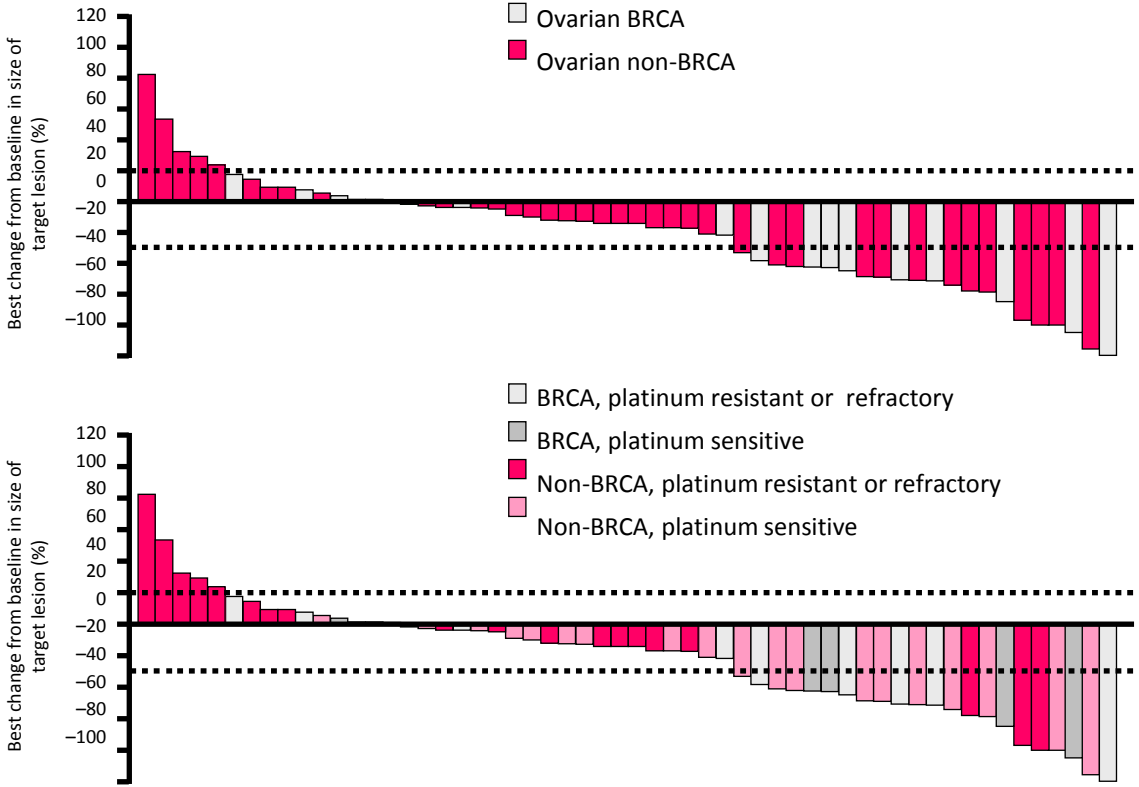
# Germline and somatic *BRCA* mutation rate in high-grade serous ovarian cancer




gBRCA, germline BRCA; HR, homologous recombination; sBRCA, somatic BRCA.

Levine, D. Personal communication;

# Olaparib in BRCA and non-BRCA ovarian cancer



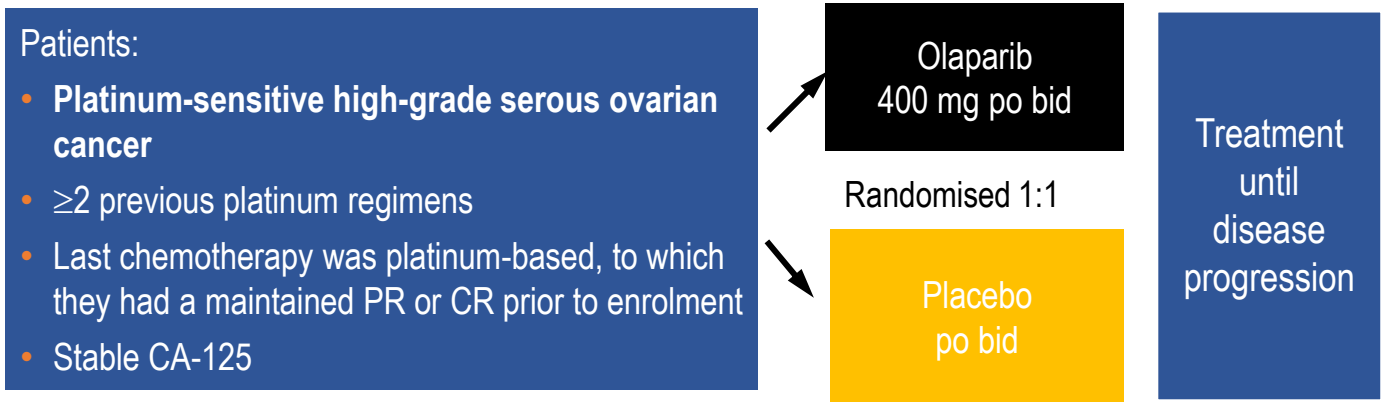

- Olaparib activity in BRCA$^{mut}$ and BRCA$^{wt}$
- Activity greater in ‘platinum-sensitive’ compared with ‘platinum-resistant’ relapse

Gelmon KA, et al. Lancet Oncol 2011;12:852–61

# Randomised trial of maintenance olaparib in platinum-sensitive high-grade serous relapsed ovarian cancer – 'study 19'

- **Aim:** **to assess the efficacy and safety of olaparib as a maintenance treatment**
- **Design:** **randomized, double-blind, placebo-controlled phase II maintenance study**

***265 patients in 82 investigational sites in 16 countries***



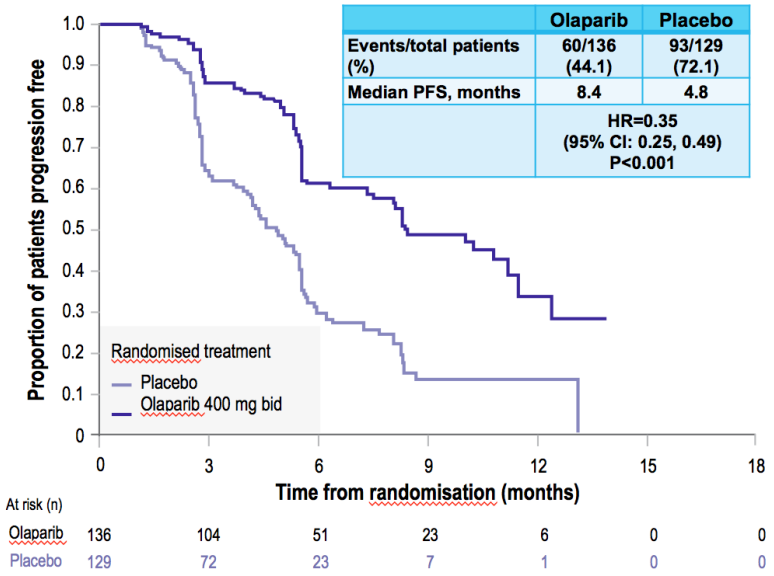

Primary end point: PFS

Sept 2008–Feb 2010
bid, twice daily; CA-125, Cancer Antigen 125;
CR, complete response; po, orally; PR, partial response.

Ledermann J et al. N Engl J Med 2012;366:1382–1392

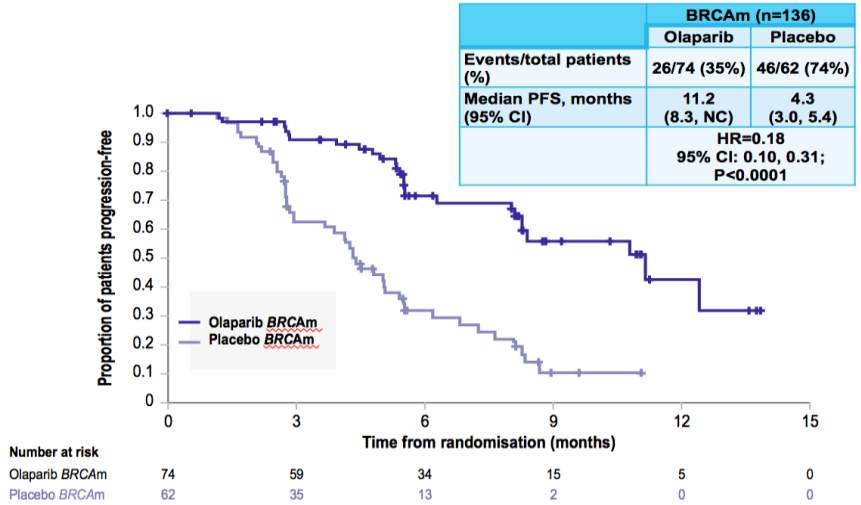
# Progression Free Survival with olaparib maintenance in 'Study 19'

Whole population with HGSOC




Ledermann J et al. N Engl J Med 2012

Subpopulation with BRCA mutation

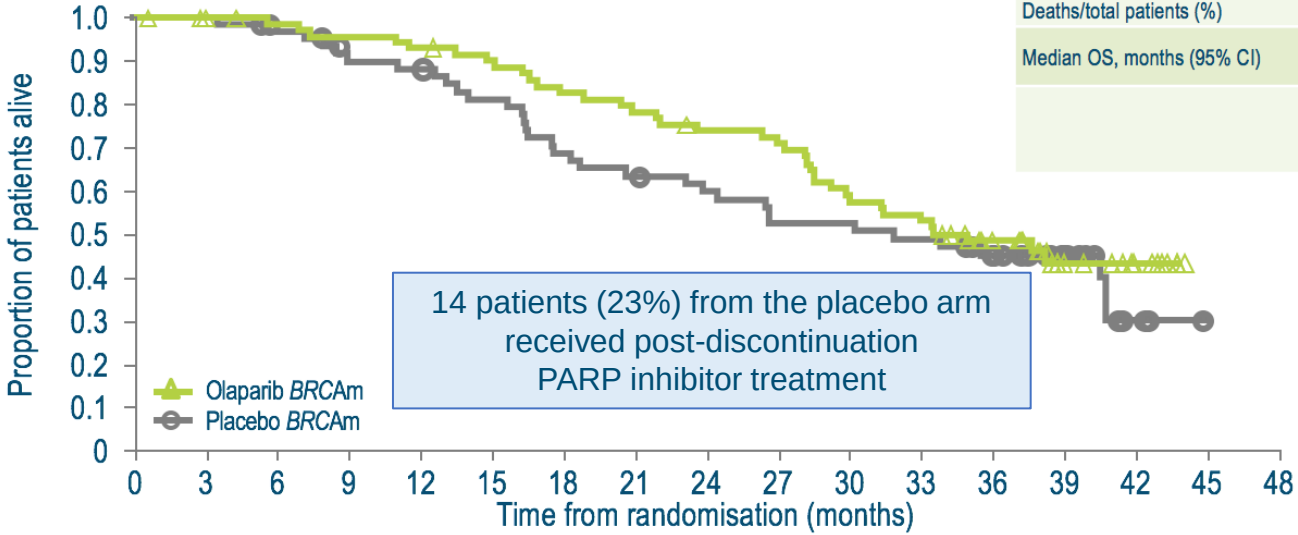



Ledermann J et al. Lancet Oncol 15:852-61 (2014)

NC, not calculable.

# Study 19 BRCAm subgroup - second interim survival analysis

| | *BRCA*m (n=136) | |
|---|---|---|
| | Olaparib | Placebo |
| Deaths/total patients (%) | 37/74 (50%) | 34/62 (55%) |
| Median OS, months (95% CI) | 34.9 (29.2, NC) | 31.9 (23.1, 40.7) |
| | HR=0.73<br>95% CI: 0.45, 1.17<br>*P*=0.19 | |




| Number at risk | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Olaparib *BRCA*m | 74 | 71 | 69 | 67 | 65 | 62 | 56 | 53 | 50 | 48 | 39 | 36 | 26 | 12 | 7 | 0 | 0 |
| Placebo *BRCA*m | 62 | 62 | 58 | 52 | 50 | 46 | 39 | 36 | 33 | 29 | 29 | 27 | 21 | 10 | 4 | 0 | 0 |

OS analysis, performed at 52% maturity

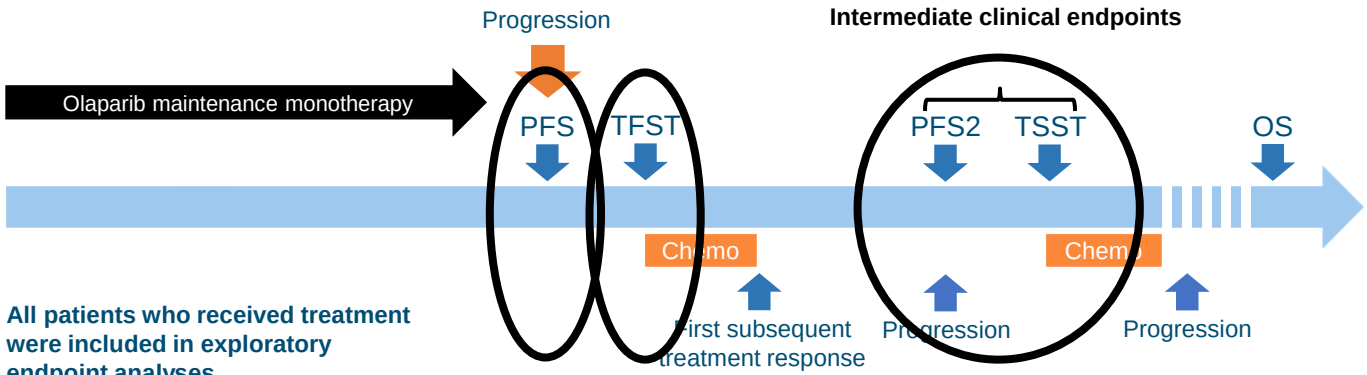
Ledermann J et al. Lancet Oncol 2014;15:852–861

# Time to First and Second Subsequent Therapy: A new exploratory endpoint

**TFST** (time from randomisation to first subsequent therapy or death)

**TSST** (time from randomisation to second subsequent therapy or death)

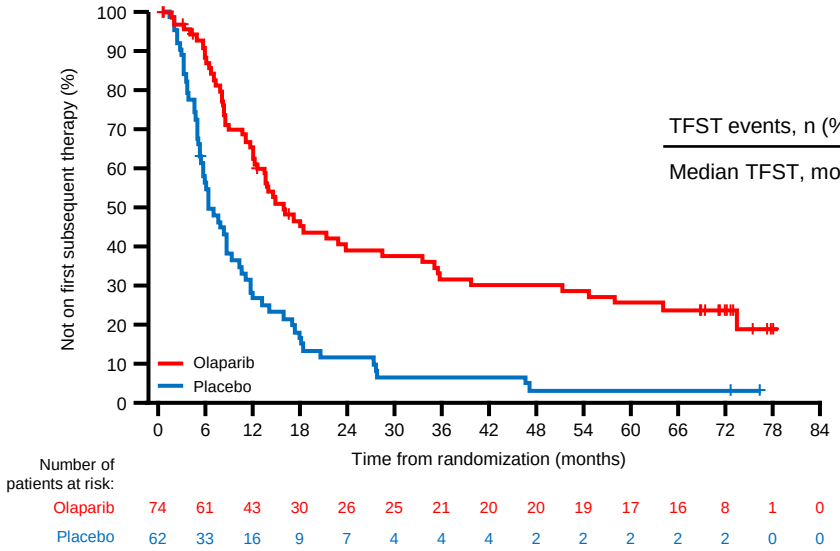
**PFS2** (time from randomisation to second objective disease progression or death)*




*TSST is a surrogate for PFS2

# Study 19: *BRCA*m population

## TFST Time to First Subsequent Treatment




| | ***BRCA*m subgroup (n=136)** | |
|---|---|---|
| | **Olaparib (n=74)** | **Placebo (n=62)** |
| TFST events, n (%) | 53 (72) | 59 (95) |
| Median TFST, months | 15.6 | 6.2 |

**HR=0.32**
**95% CI 0.22–0.48**
***P*<0.00001**

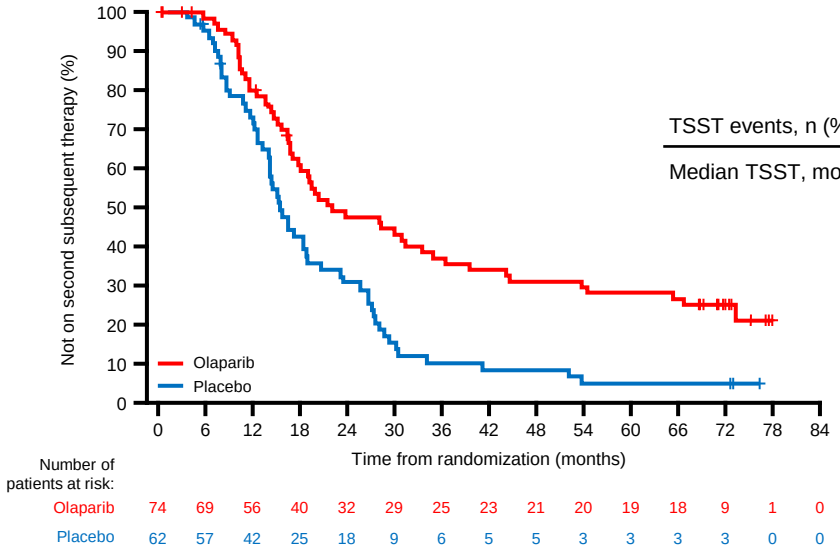
Maturity: 82%

Updated exploratory analysis

Ledermann et al ASCO 2016

# Study 19: *BRCA*m patients – maintenance olaparib

## TSST Time to Second Subsequent Treatment




| | ***BRCA*m subgroup (n=136)** | |
|---|---|---|
| | **Olaparib (n=74)** | **Placebo (n=62)** |
| TSST events, n (%) | 52 (70) | 56 (90) |
| Median TSST, months | 22.0 | 15.3 |

**HR=0.41**
**95% CI 0.28–0.62**
***P*=0.00001**

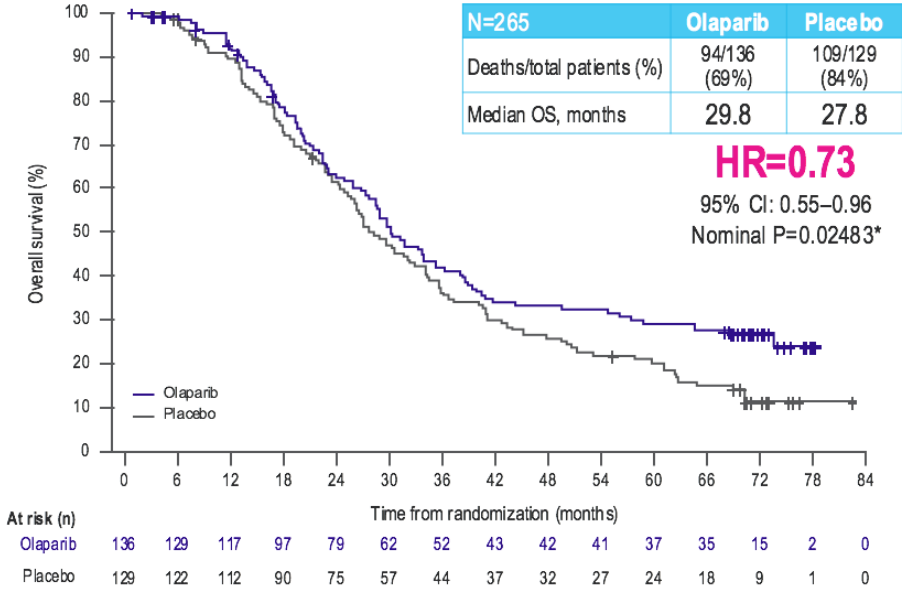
Maturity: 79%

14 patients (23%) from the placebo arm received post-discontinuation PARP inhibitor treatment

Updated exploratory analysis

Ledermann et al ASCO 2016

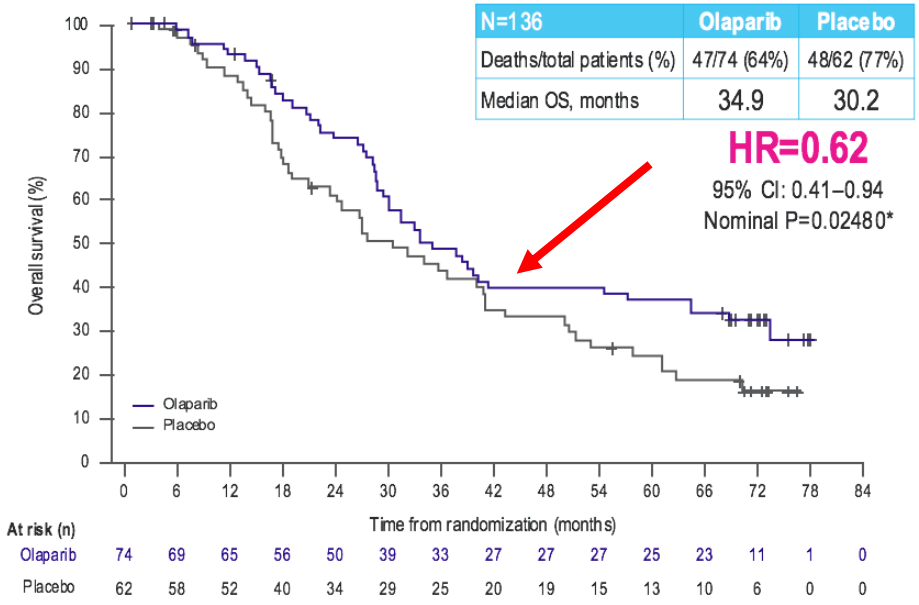
# Updated survival of Study 19- maintenance olaparib




Maturity 77 %

Whole study population

BRCAm subgroup

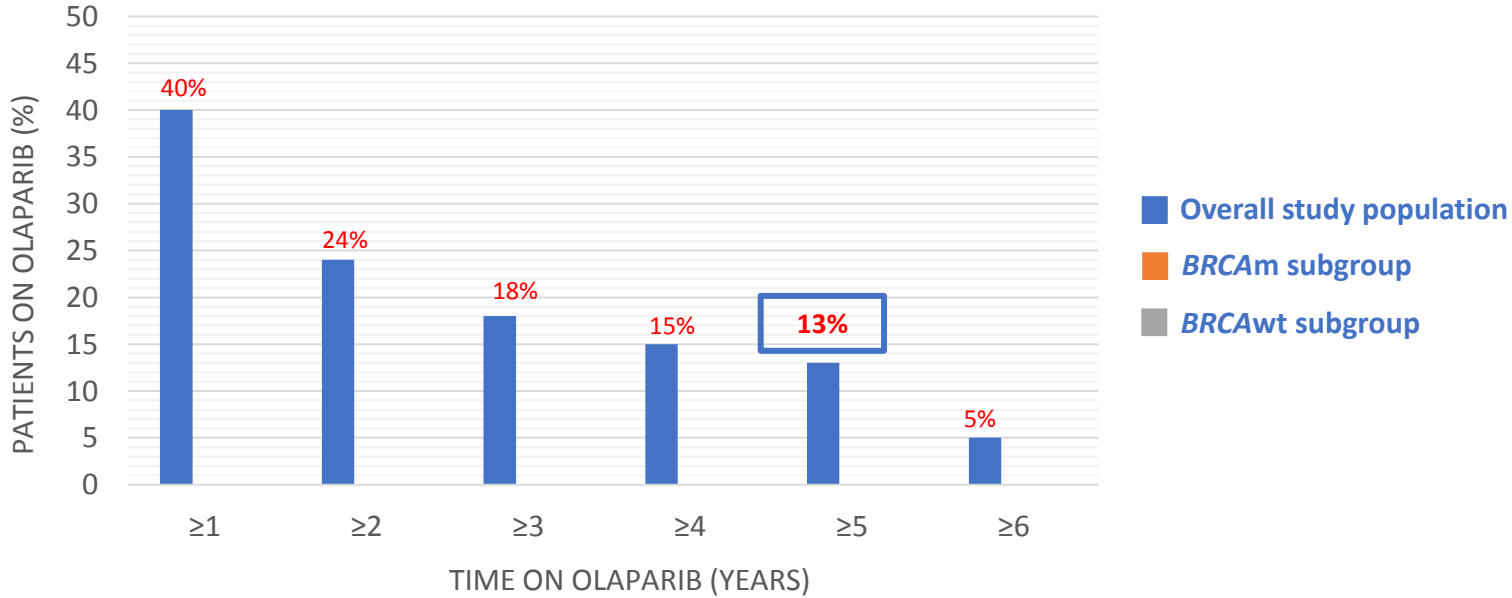



Maturity 70%

Ledermann et al ASCO 2016; Lancet Oncol 2016

# Long-term exposure to olaparib in ‘study 19’ in BRCAm and BRCA$^{wt}$

Median follow-up of 5.9 years: **15 patients (11%)** still receiving **olaparib** (**8 *BRCA*m**, 7 *BRCA*wt); one patient (<1%) still receiving placebo (*BRCA*m)




Ledermann et al ASCO 2016

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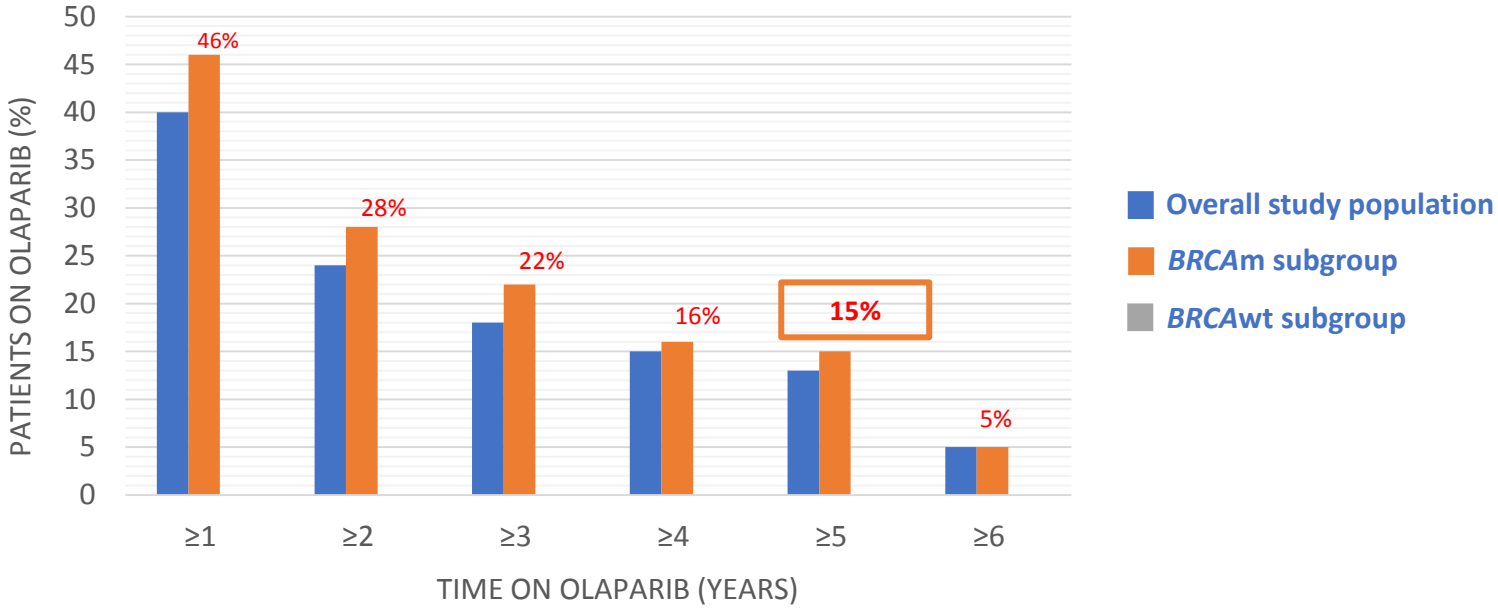


Ledermann et al ASCO 2016

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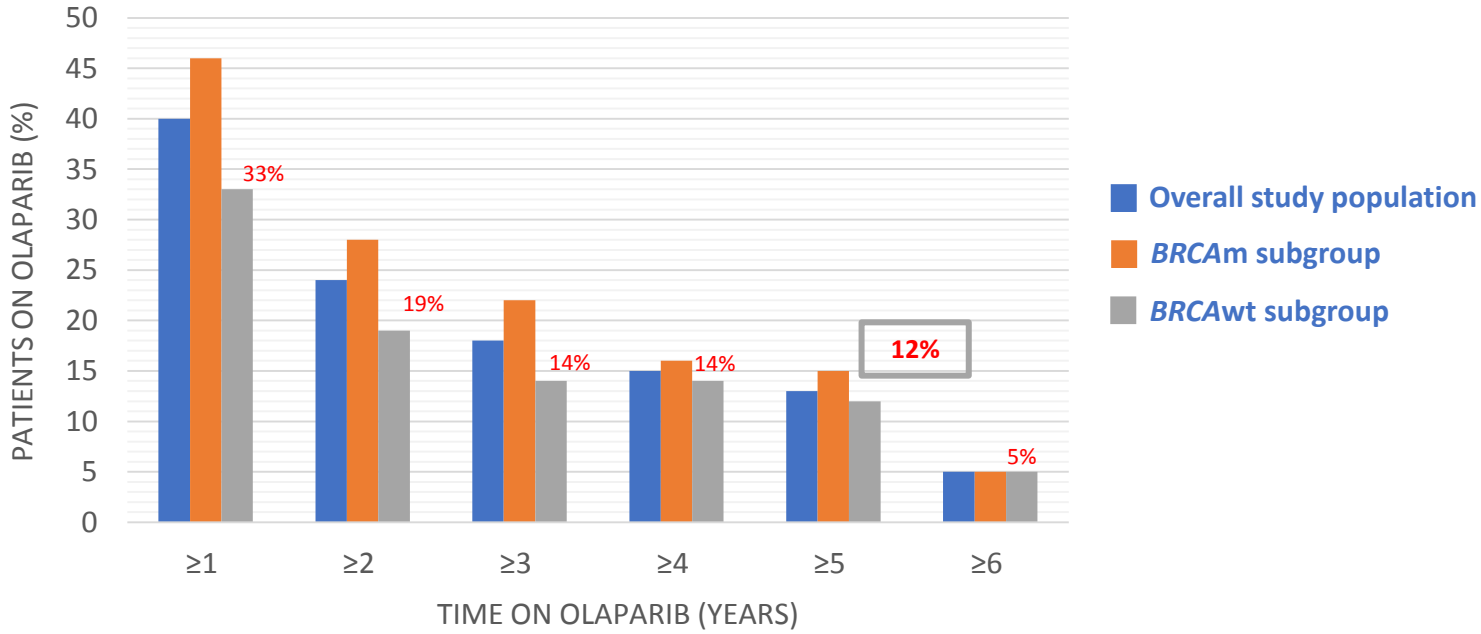
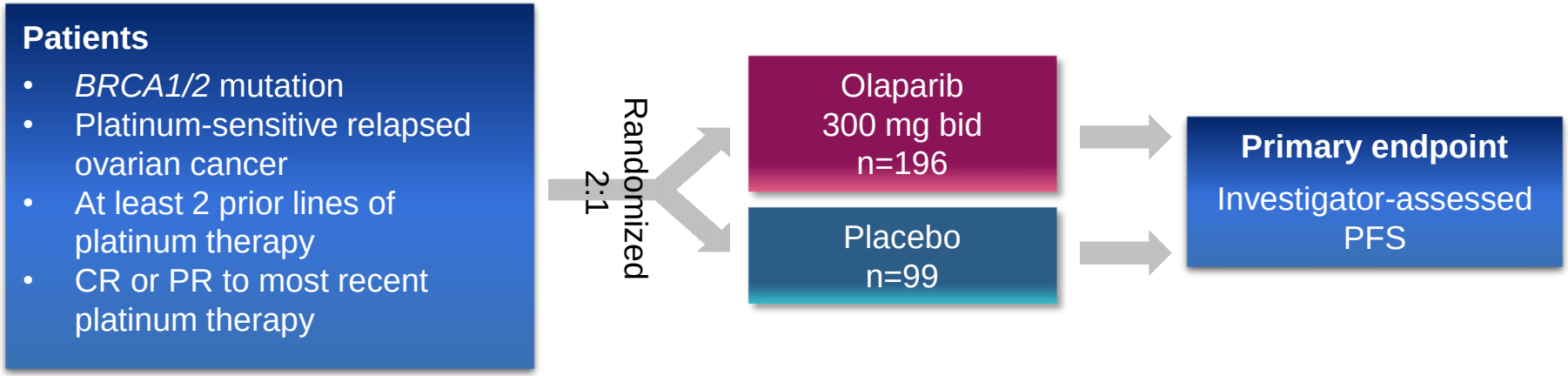



Ledermann et al ASCO 2016

# SOLO2/ENGOT-Ov21: study design




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

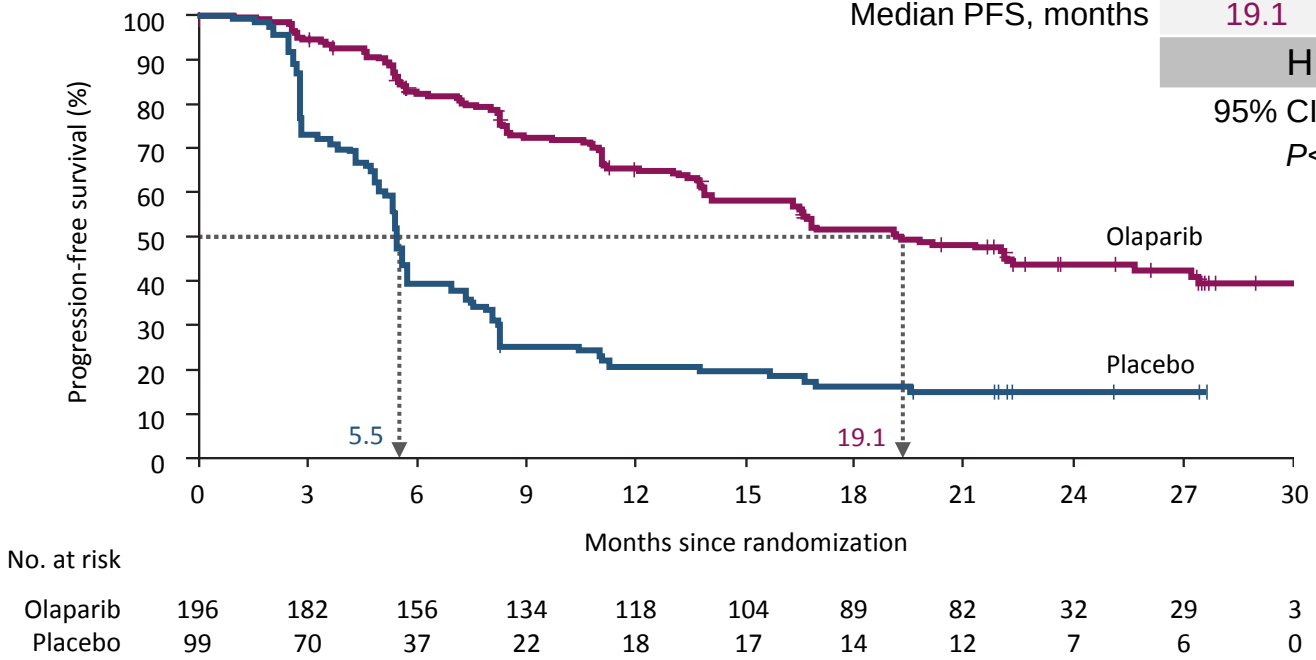
- Key secondary endpoints:
  - Time to first subsequent therapy or death (TFST), time to second progression (PFS2), time to second subsequent therapy or death (TSST), overall survival (OS)
  - Safety, health-related quality of life (HRQoL*)

Pujade-Lauraine et al SGO 2017

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

# SOLO-2 PFS by investigator assessment

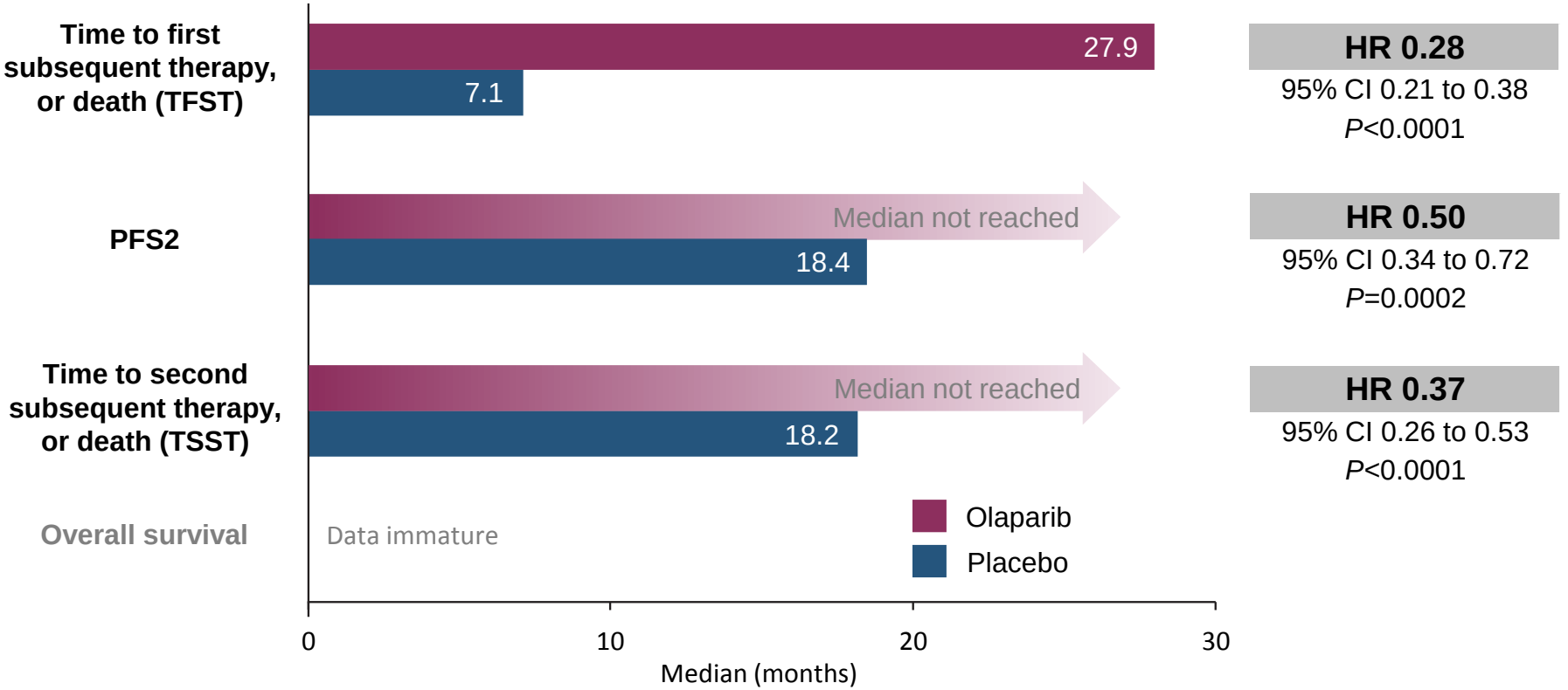
| | Olaparib (n=196) | Placebo (n=99) |
|---|---|---|
| Events (%) | 107 (54.6) | 80 (80.8) |
| Median PFS, months | 19.1 | 5.5 |
| HR 0.30 | | |
| 95% CI 0.22 to 0.41 | | |
| *P*<0.0001 | | |




Median follow-up was 22.1 months in the olaparib group and 22.2 months for placebo

Pujade-Lauraine et al SGO 2017

# Secondary efficacy endpoints- SOLO2



# SOLO-2: Total adverse events

| Characteristic, n (%) | Olaparib (n=195) | Placebo (n=99) |
|---|---|---|
| Any AE | 192 (98.5) | 94 (94.9) |
| Any AE grade ≥3 | 72 (36.9) | 18 (18.2) |
| Any SAE | 35 (17.9) | 8 (8.1) |
| Any AE leading to dose reduction | 49 (25.1) | 3 (3.0) |
| Any AE leading to discontinuation of study treatment | 21 (10.8) | 2 (2.0) |
| Any AE with an outcome of death | 1 (0.5) | 0 |

AE, adverse event; SAE, serious adverse event

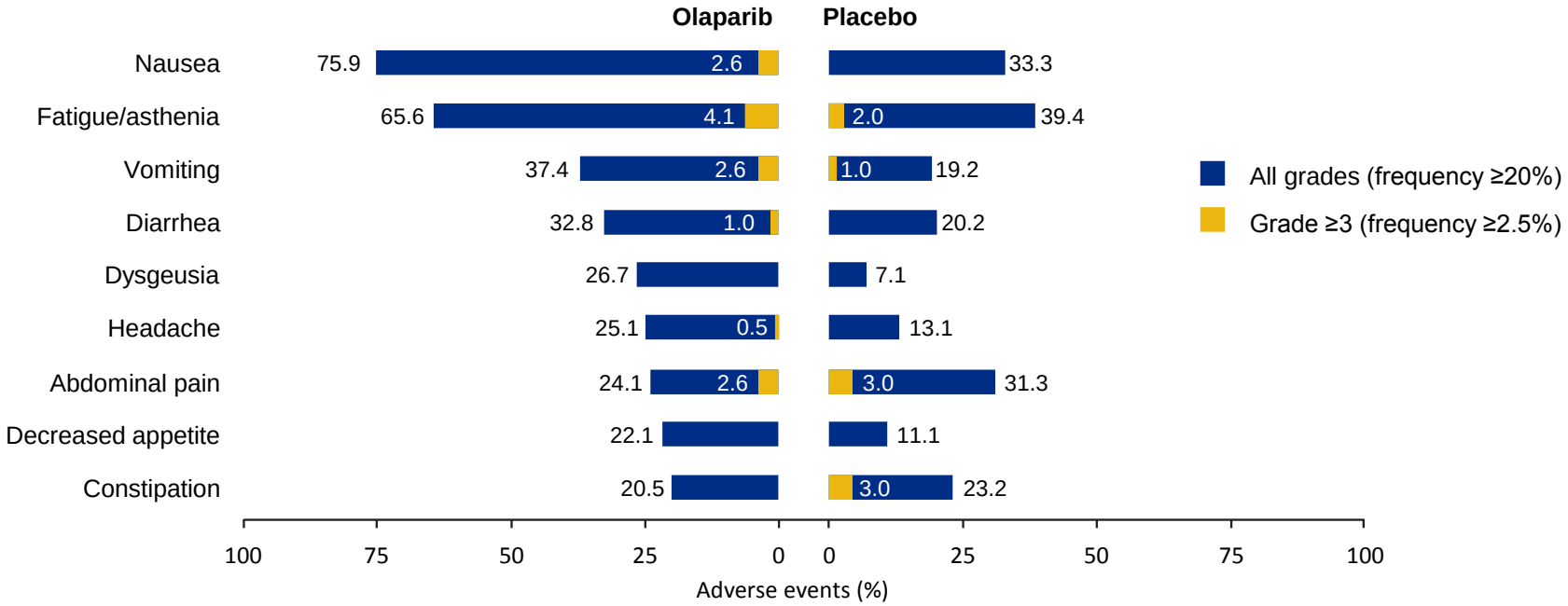
# Most common hematologic adverse events

| Event, n (%) | Olaparib (n=195) | | Placebo (n=99) | |
|---|---|---|---|---|
| | All grades | Grade ≥3 | All grades | Grade ≥3 |
| Anemia* | 85 (43.6) | 38 (19.5) | 8 (8.1) | 2 (2.0) |
| Neutropenia* | 38 (19.5) | 10 (5.1) | 6 (6.1) | 4 (4.0) |
| Thrombocytopenia* | 27 (13.8) | 2 (1.0) | 3 (3.0) | 1 (1.0) |

MDS/AML: 4 cases in olaparib group (2.1%), including one case of CMML
4 cases in placebo group (4.0%)

*Grouped terms

# Most common non-hematologic adverse events




Other AEs of interest

Elevated ALT: 10 patients in olaparib group (5.1%) vs 4 patients in placebo group (4.0%)

Elevated AST: 4 patients in olaparib group (2.1%) vs 4 patients in placebo group (4.0%)

# NOVA trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer

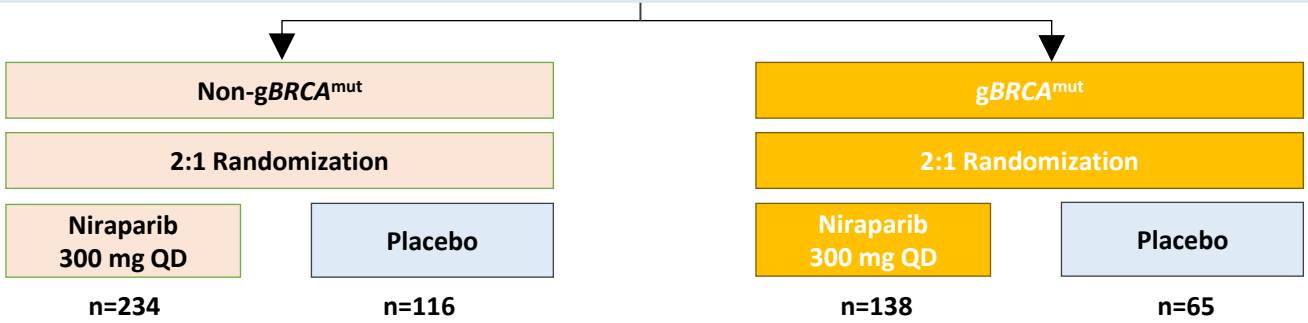
M.R. Mirza, B.J. Monk, J. Herrstedt, A.M. Oza, S. Mahner, A. Redondo, M. Fabbro, J.A. Ledermann, D. Lorusso, I. Vergote, N.E. Ben-Baruch, C. Marth, R. Mądry, R.D. Christensen, J.S. Berek, A. Dørum, A.V. Tinker, A. du Bois, A. González-Martín, P. Follana, B. Benigno, P. Rosenberg, L. Gilbert, B.J. Rimel,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

N Engl J Med 2016;375:2154-64

# NOVA: Maintenance Niraparib in Recurrent Platinum-Sensitive High-Grade Serous Ovarian Cancer

- **Phase III, multicenter, randomized, double-blind, placebo-controlled study**
- Relapsed high-grade serous histology or known g*BRCA*$^{mut}$
- ≥2 prior regimens of platinum-based chemotherapy
- **Responded to last platinum regimen; remains in response and enrolled within 8 weeks of completion of last platinum regimen**
- **No measurable lesion ≥2cm**

N=553

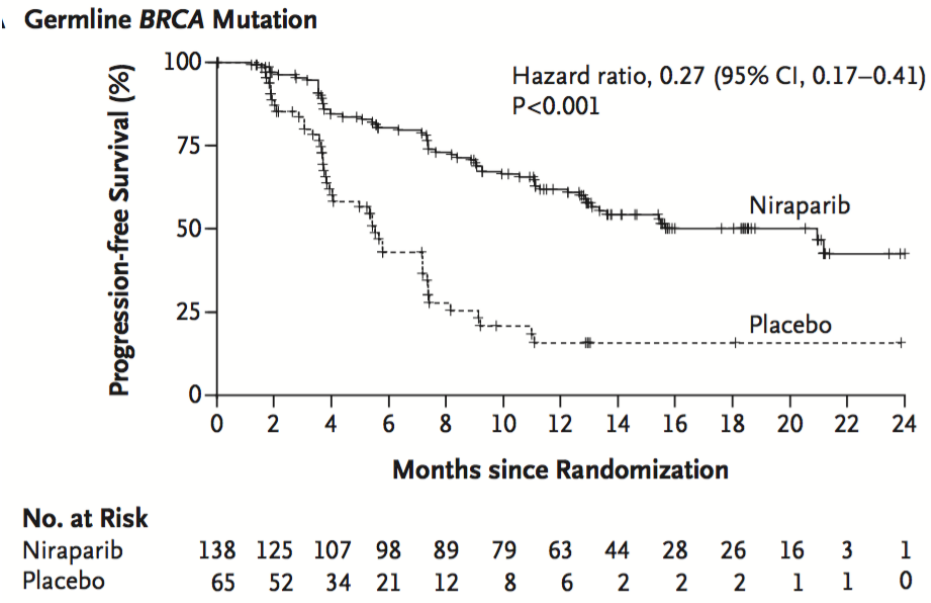


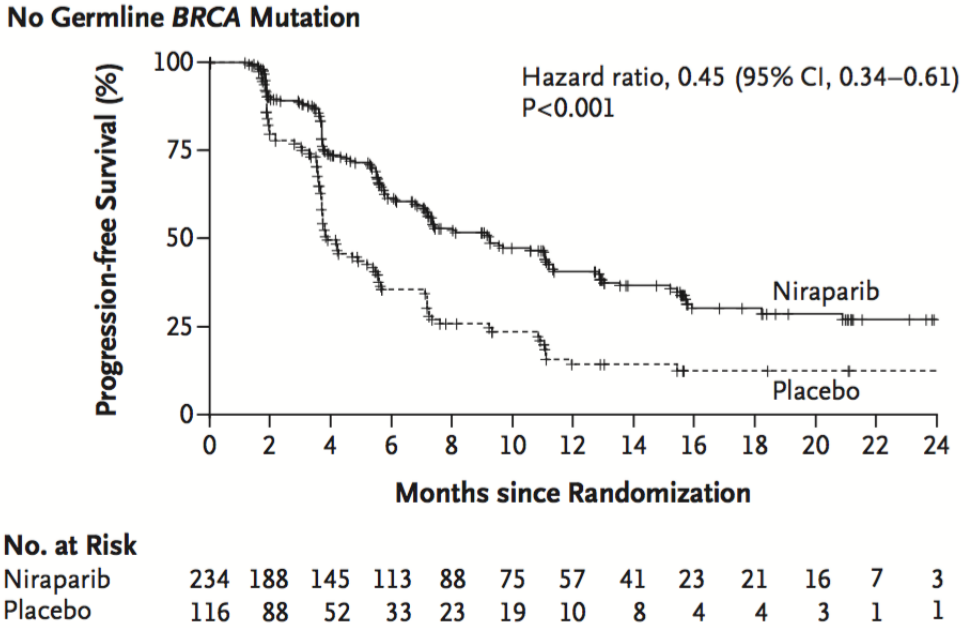

**Primary Endpoint**

- PFS; >90% power to detect 4.8-month improvement (HR 0.50)
- Non-g*BRCA*$^{mut}$ cohort endpoint assessed hierarchically to control type 1 error: HRD+ population first, followed by entire population

Mirza et al NEJM 2016

# NOVA trial- niraparib – Primary outcome

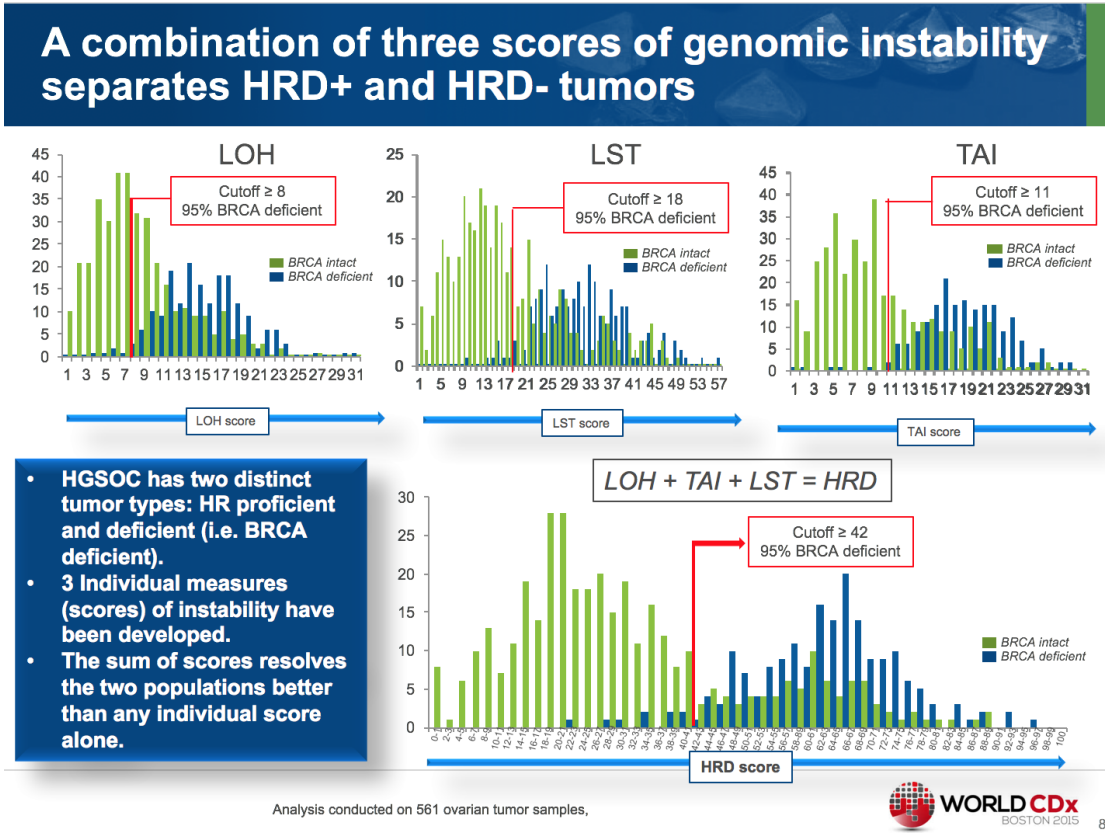



Mirza et a;l NEJM 2016

# Testing for Homologous Recombination Deficiency (HRD)

- **Loss of Heterozygosity,**
- **Large-scale State Transitions,**
- **Telomeric Imbalance**



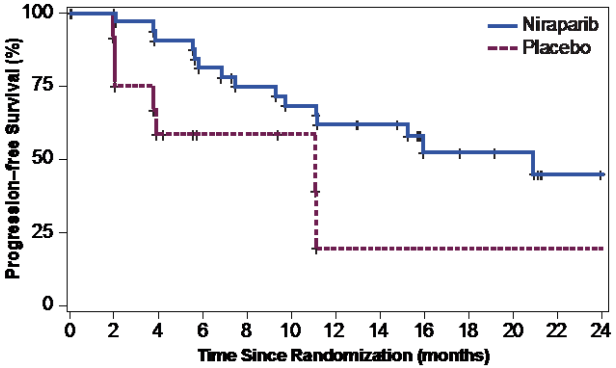

Courtesy of Tesaro/Myriad Genetics

# NOVA: Exploratory Analysis: PFS in non-gBRCAmut Subgroups

## HRD-positive

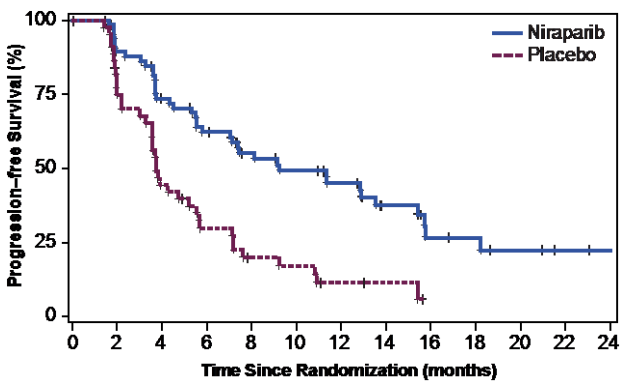
### sBRCAmut

| Treatment | PFS Median (95% CI) (Months) | Hazard Ratio (95% CI) p value | % of Patients without Progression or Death | |
|---|---|---|---|---|
| | | | 12 mo | 18 mo |
| Niraparib (N=35) | **20.9** (9.7, NR) | **0.27** (0.081, 0.903) p=0.0248 | 62% | **52%** |
| Placebo (N=12) | **11.0** (2.0, NR) | | 19% | 19% |



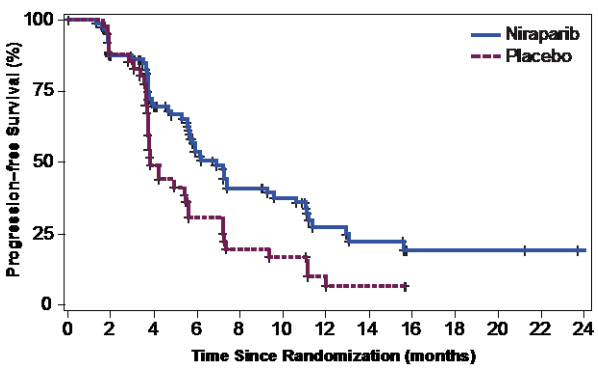

### BRCAwt

| Treatment | PFS Median (95% CI) (Months) | Hazard Ratio (95% CI) p value | % of Patients without Progression or Death | |
|---|---|---|---|---|
| | | | 12 mo | 18 mo |
| Niraparib (N=71) | **9.3** (5.8, 15.4) | **0.38** (0.231, 0.628) p=0.0001 | 45% | **27%** |
| Placebo (N=44) | **3.7** (3.3, 5.6) | | 11% | 6% |




## HRD-negative

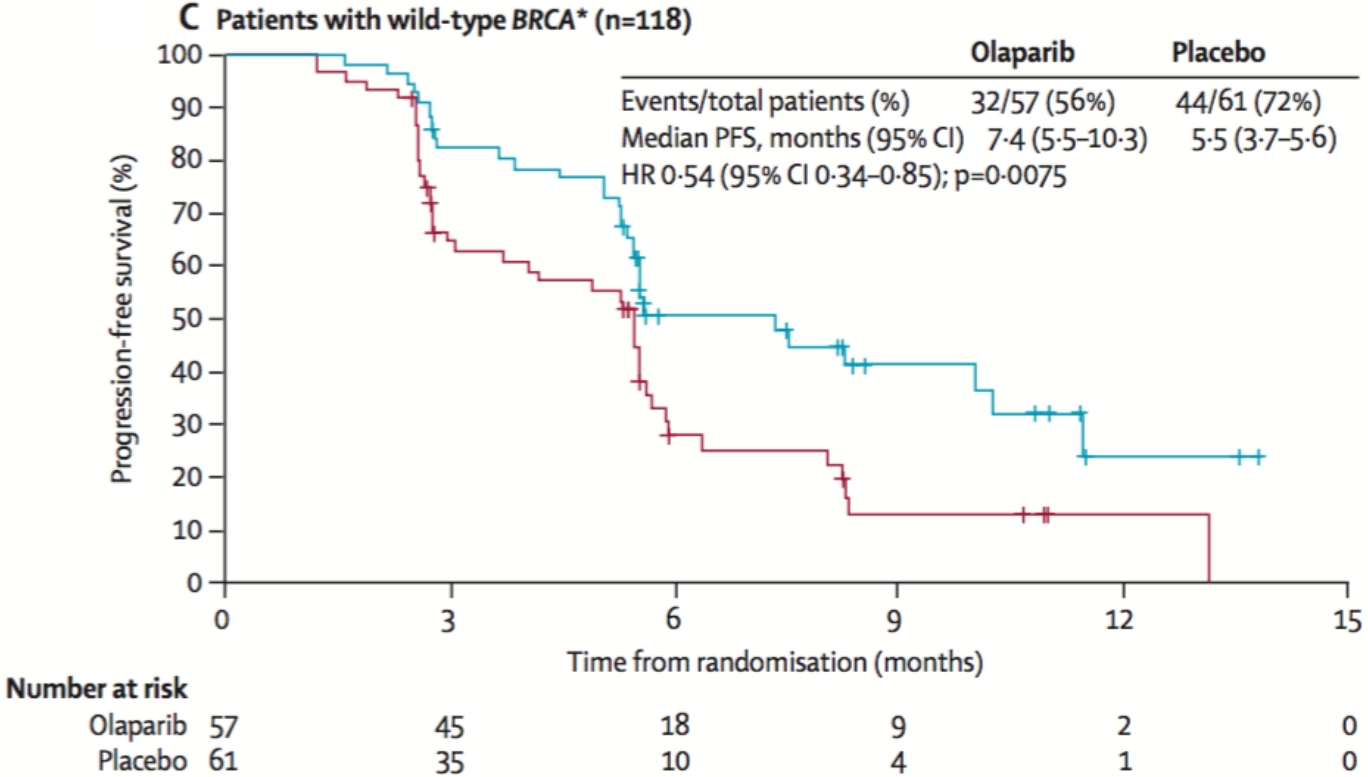
| Treatment | PFS Median (95% CI) (Months) | Hazard Ratio (95% CI) p value | % of Patients without Progression or Death | |
|---|---|---|---|---|
| | | | 12 mo | 18 mo |
| Niraparib (N=92) | **6.9** (5.6, 9.6) | **0.58** (0.361, 0.922) p=0.0226 | 27% | **19%** |
| Placebo (N=42) | **3.8** (3.7, 5.6) | | 7% | 7% |




NR=Not reached

Mirza et al ESMO 2016

# Olaparib Study 19
# Progression-free survival in BRCA$^{wt}$ (excludes gBRCA & sBRCA)




BRCAwt, wild type (includes patients with no known BRCAm or a mutation of unknown significance)

Ledermann et al Lancet Oncol 2014

# How well are PARP inhibitors tolerated?

- Key side effects
- Dose modification
- Early discontinuation due to Adverse Events
- Quality of Life measurements on maintenance therapy

# NOVA trial- Niraparib- Safety profile

| Event | Niraparib (N = 367) | | Placebo (N = 179) | |
|---|---|---|---|---|
| | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 |
| | *number of patients (percent)* | | | |
| Nausea | 270 (73.6) | 11 (3.0) | 63 (35.2) | 2 (1.1) |
| Thrombocytopenia† | 225 (61.3) | 124 (33.8) | 10 (5.6) | 1 (0.6) |
| Fatigue‡ | 218 (59.4) | 30 (8.2) | 74 (41.3) | 1 (0.6) |
| Anemia§ | 184 (50.1) | 93 (25.3) | 12 (6.7) | 0 |
| Constipation | 146 (39.8) | 2 (0.5) | 36 (20.1) | 1 (0.6) |
| Vomiting | 126 (34.3) | 7 (1.9) | 29 (16.2) | 1 (0.6) |
| Neutropenia¶ | 111 (30.2) | 72 (19.6) | 11 (6.1) | 3 (1.7) |
| Headache | 95 (25.9) | 1 (0.3) | 17 (9.5) | 0 |
| Decreased appetite | 93 (25.3) | 1 (0.3) | 26 (14.5) | 1 (0.6) |
| Insomnia | 89 (24.3) | 1 (0.3) | 13 (7.3) | 0 |
| Abdominal pain | 83 (22.6) | 4 (1.1) | 53 (29.6) | 3 (1.7) |
| Dyspnea | 71 (19.3) | 4 (1.1) | 15 (8.4) | 2 (1.1) |
| Hypertension | 71 (19.3) | 30 (8.2) | 8 (4.5) | 4 (2.2) |
| Diarrhea | 70 (19.1) | 1 (0.3) | 37 (20.7) | 2 (1.1) |
| Dizziness | 61 (16.6) | 0 | 13 (7.3) | 0 |

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# NOVA Trial Niraparib: Treatment-emergent Grade 3/4 Adverse Events occurring in ≥5% patients

| Event — no. (%) | Niraparib (N=367) | Placebo (N=179) |
|---|---|---|
| **Thrombocytopenia[a]** | 124 (33.8) | 1 (0.6) |
| **Anemia[b]** | 93 (25.3) | 0 |
| **Neutropenia[c]** | 72 (19.6) | 3 (1.7) |
| **Fatigue[d]** | 30 (8.2) | 1 (0.6) |
| **Hypertension** | 30 (8.2) | 4 (2.2) |

**MDS/AML occurred in 5 of 367 (1.4%) in patients who received niraparib and 2 of 179 (1.1%) in patients who received placebo.**

*There were no Grade 5 events.

Mirza et al ESMO 2016

# Olaparib study 19 and niraparib NOVA : Dose reductions and discontinuation due to side effects

| | Olaparib | Placebo |
|---|---|---|
| SAE | 25 (18%) | 11 (9%) |
| AE Leading to dose interruptions | 49 (36%) | 21 (16%) |
| AE leading to dose reduction | 59 (43%) | 29 (23%) |
| AE leading to treatment discontinuation | 8 (6%) | 2 (2%) |

Ledermann et al Lancet Oncol 2016

| | Niraparib | Placebo |
|---|---|---|
| SAE | 110 ( 30%) | 27 ( 15%) |
| AE leading to dose interruptions | 253 (69%) | 9 (5%) |
| AE leading to dose reduction | 244 (65%) | 26 (15%) |
| AE leading to treatment discontinuation | 54 ( 15%) | 4 (2%) |

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# Current perspectives on use of PARP inhibitors for maintenance

- Clear evidence of benefit of maintenance olaparib and niraparib in BRCA mutated platinum-sensitive ovarian cancer
- Both drugs active in non-BRCA-mutated ovarian cancers
- FDA license for niraparib includes all patients with platinum-sensitive recurrence responding to platinum-based therapy. EMA review not completed
  - Both gBRCA and non gBRCA subgroups – significant PFS benefit
- Long-term F/U data for olaparib maintenance shows benefit beyond 5 years in 15% women with BRCAm and 12% without BRCAm
- Implications for testing for BRCA mutation?

# Single Agent Therapy- an alternative?

# Clear evidence of benefit of olaparib monotherapy in BRCA-mutated ovarian cancer

| Response | Ovarian (n = 193) No. | % |
|---|---|---|
| Tumor response rate | 60 | 31.1 |
| 95% CI | 24.6 to 38.1 | |
| CR* | 6 | 3 |
| PR* | 54 | 28 |
| Stable disease ≥ 8 weeks | 78 | 40 |
| 95% CI | 33.4 to 47.7 | |
| Stable disease | 64 | 33 |
| Unconfirmed PR | 12 | 6 |
| PD† | 41 | 21 |
| 95% CI | 15.7 to 27.7 | |
| RECIST progression | 33 | 17 |
| Early death‡ | 8 | 4 |
| Not evaluable | 14 | 7 |
| No follow-up assessments | 12 | 6 |
| Stable disease < 8 weeks | 2 | 1 |

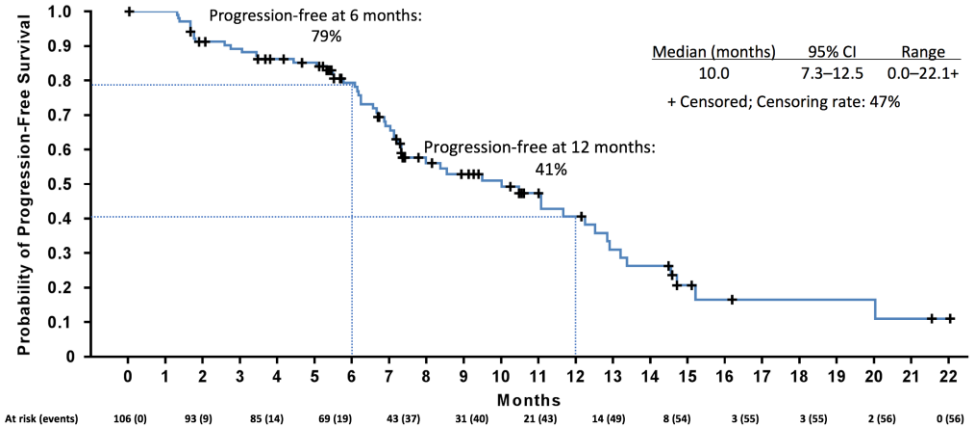
Kaufman et al J Clin Oncol 2014

**Table 1.** Objective response and DOR in patients with g*BRCA*-mutated advanced ovarian cancer who received three or more prior lines of chemotherapy in Study 42

| | ***N* = 137** |
|---|---|
| Objective response rate (95% CI) | 34% (26–42) |
| Complete response | 2% |
| Partial response | 32% |
| Median DOR in months (95% CI) | 7.9 (5.6–9.6) |

**19 December 2014: FDA licensed Olaparib for the treatment of BRCA-mutated (BRACAnalysis CDx™) ovarian cancer in patients who have received ≥3 prior lines of therapy**

# Rucaparib- gBRCA/sBRCA




**19 December 2016: FDA- Accelerated approval in patients with a BRCA mutation (FoundationFocus™ CDx*BRCA)* who have received 2 or more prior lines**

Study 10 Part 2a (30 Nov 2015) and ARIEL2 (29 Feb 2016).

75% platinum-sensitive
Median prior platinum lines = 2

| Parameter | Study 10 n=42 | ARIEL2 n=64 | Efficacy population n=106 |
|---|---|---|---|
| | n (%) [95% CI] | | |
| **Investigator-assessed RECIST ORR (confirmed CR+PR)** | **25 (59.5) [43.3–74.4]** | **32 (50.0) [37.2–62.8]** | **57 (53.8) [43.8–63.5]** |
| CR | 4 (9.5) | 5 (7.8) | 9 (8.5) |
| PR | 21 (50.0) | 27 (42.2) | 48 (45.3) |
| SD | 12 (28.6) | 24 (37.5) | 36 (34.0) |
| PD | 2 (4.8) | 7 (10.9) | 9 (8.5) |
| NE | 3 (7.1) | 1 (1.6) | 4 (3.8) |
| **Investigator-assessed RECIST/GCIG CA-125 ORR** | | | **75 (70.8) [61.1–79.2]** |

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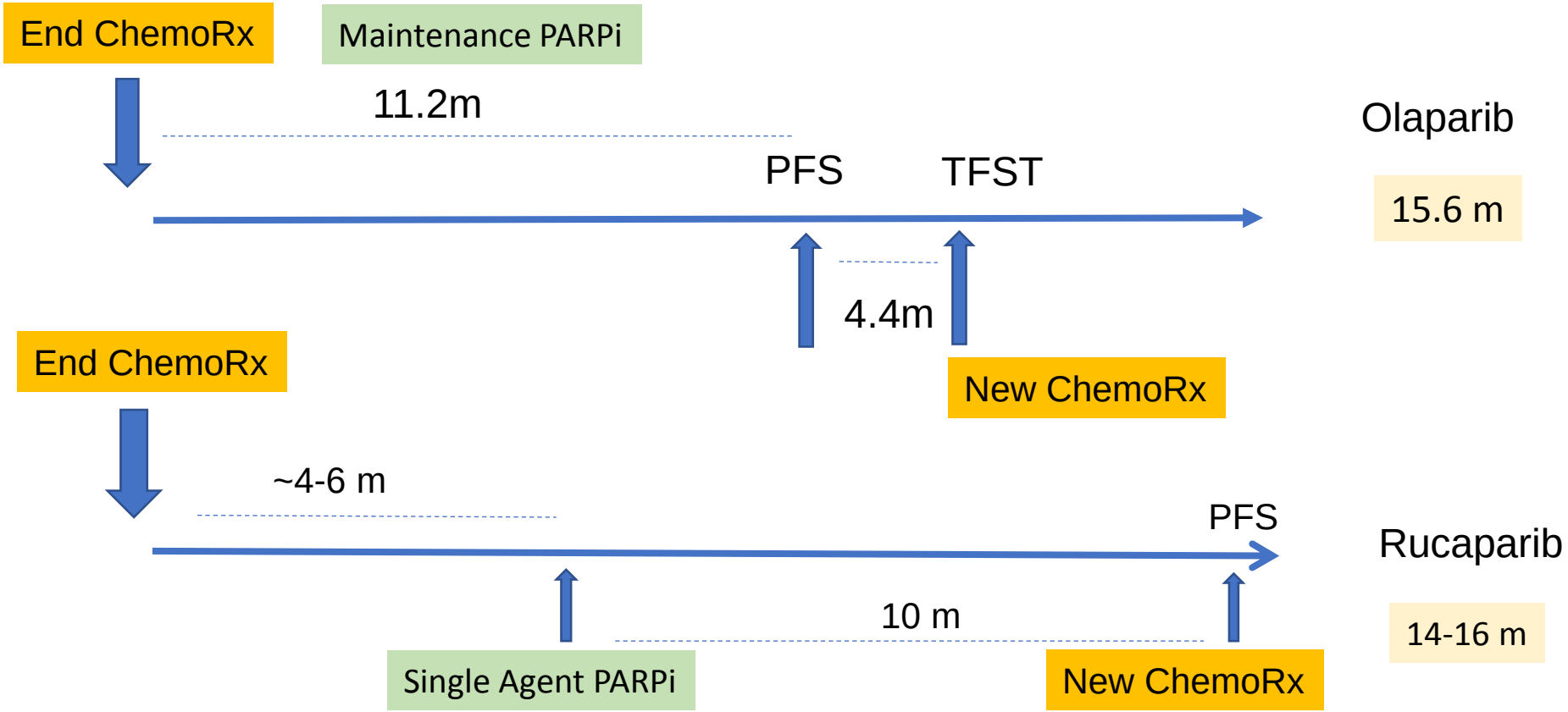
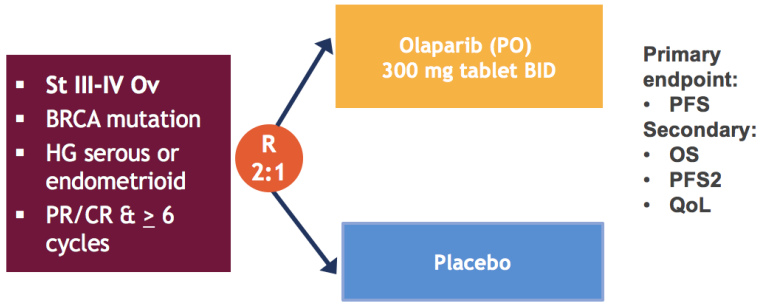
# Maintenance *versus* single agent?
# Two strategies for the use of PARP inhibitors



# Extending the options for PARP inhibitor therapy

# First Line - maintenance in Ovarian Cancer

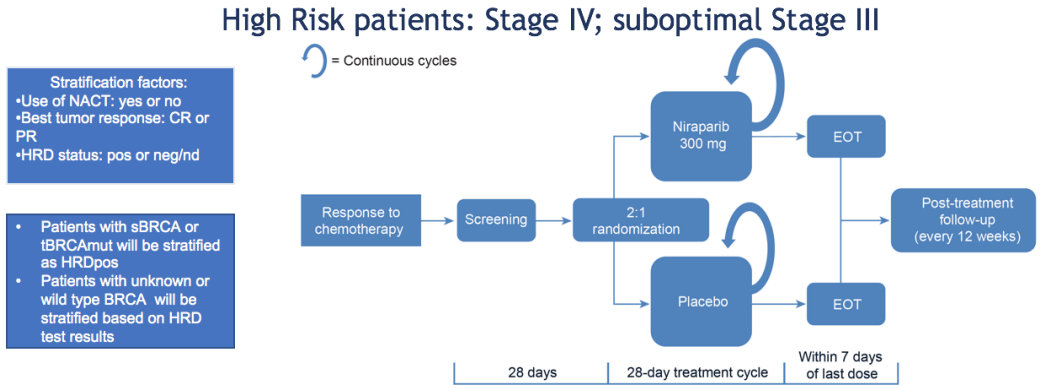
## SOLO-1- in BRCAm




Estimated Enrollment: 397
Study Start Date: Aug 2013
Estimated Study Completion Date: Jan 2022
Estimated enroll Completion: Jul 2016 (Final data)

ClinicalTrials.gov Id NCT01844986

## PRIMA: Niraparib in Ovarian Cancer




**Primary Endpoint**
**PFS in HRDpos patients; hierarchical analysis for all patients regardless of HRD status**
Secondary:
OS, Patient Reported Outcomes (PRO's), tTme to First Subsequent Treatment, PFS2, safety and tolerability of study therapy

# Trials with PARP inhibitors – awaited results

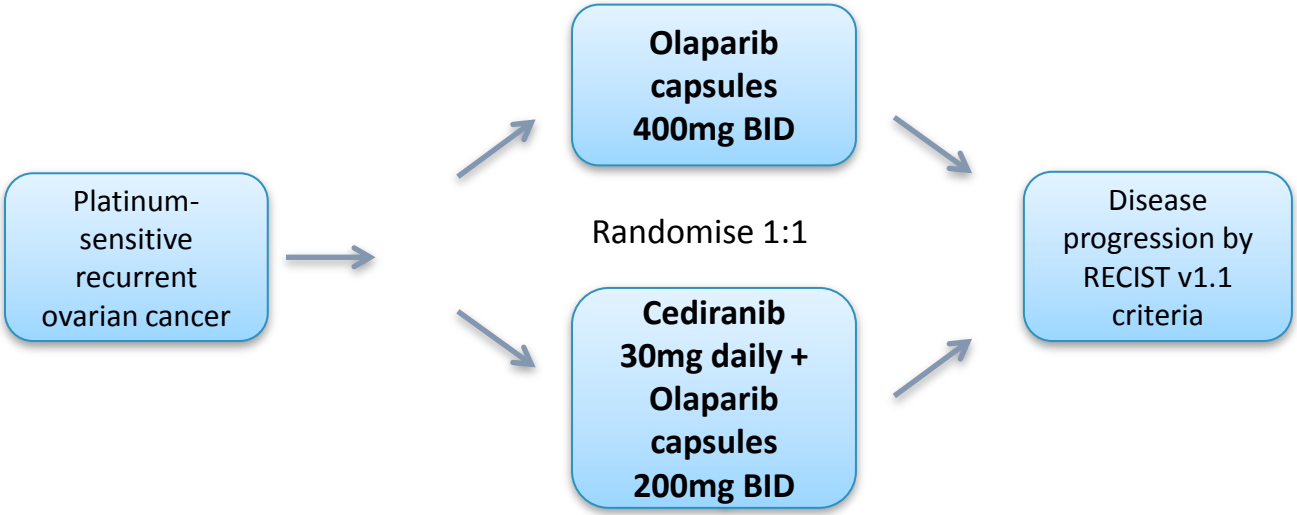
| PARP Inhibitor | Company | Target PARP | Summary |
|---|---|---|---|
| Olaparib (AZD2281) | AstraZeneca | PARP1/2/3 | Phase III trials with tablet formulation - 1st line and recurrence **(SOLO-1)** |
| Rucaparib (AG-014699; CO-338) | Clovis Oncology | PARP1/2 | Phase III trial in BRCAm, BRCAwt **(ARIEL3)** with HRD analysis with Foundation Medicine |
| Veliparib (ABT-888) | Abbvie | PARP1/2 | 1st line phase III **GOG 3005** with chemotherapy and maintenance |
| Niraparib (MK4827) | Tesaro | PARP1/2 | 1st line phase III trial- **Prima** |
| Talazoparib (BMN-673) | BioMarin/ Medivation | PARP1/2 | Ovarian cancer strategy unclear |

# Future Directions- ‘second generation’ studies

# Combining olaparib with cediranib

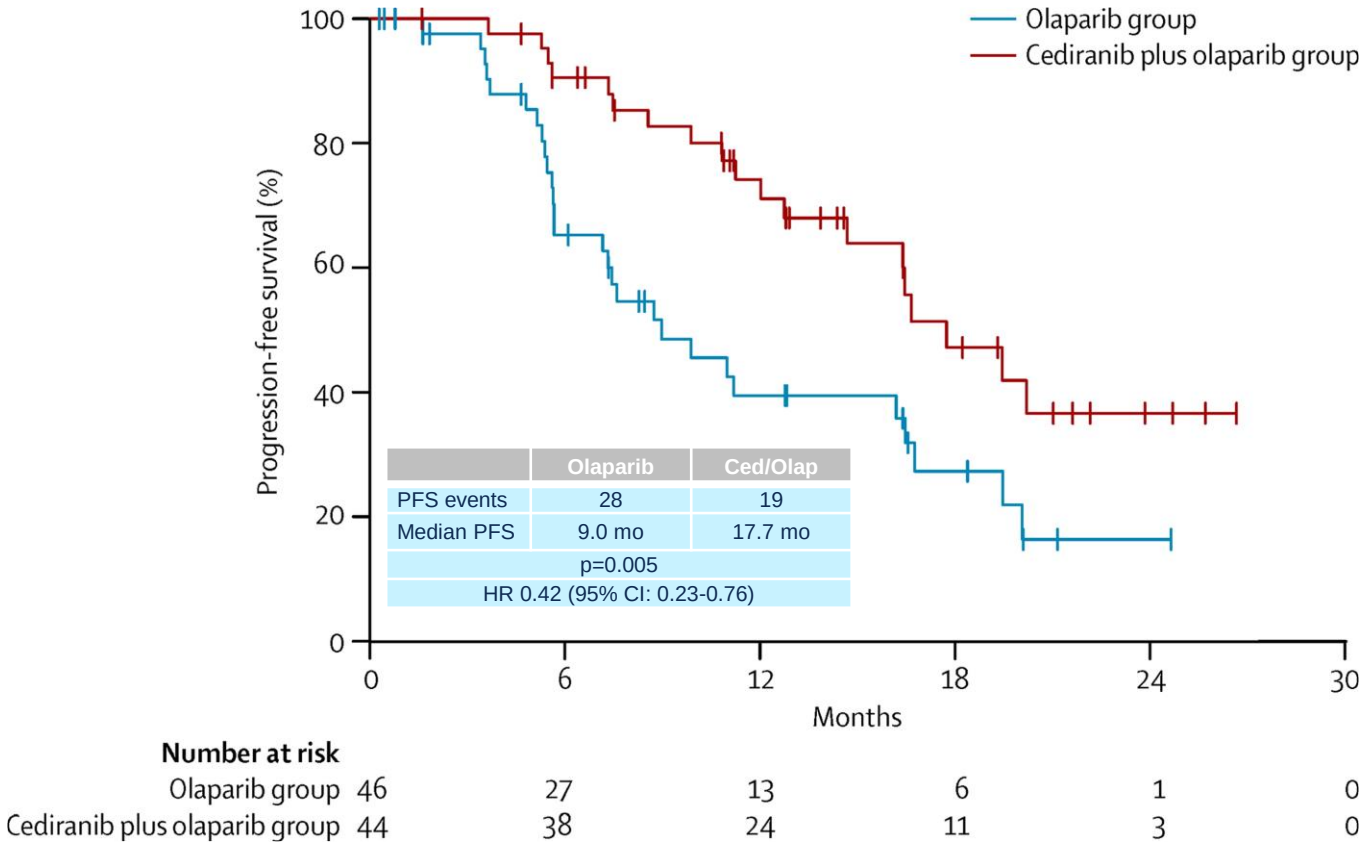
## Hypothesis: inhibiting angiogenesis increases the degree of HRD

- Phase 2 open-label randomized study
- Platinum-sensitive recurrent ovarian, fallopian tube, or primary peritoneal cancer
- Olaparib ± cediranib continued to progression



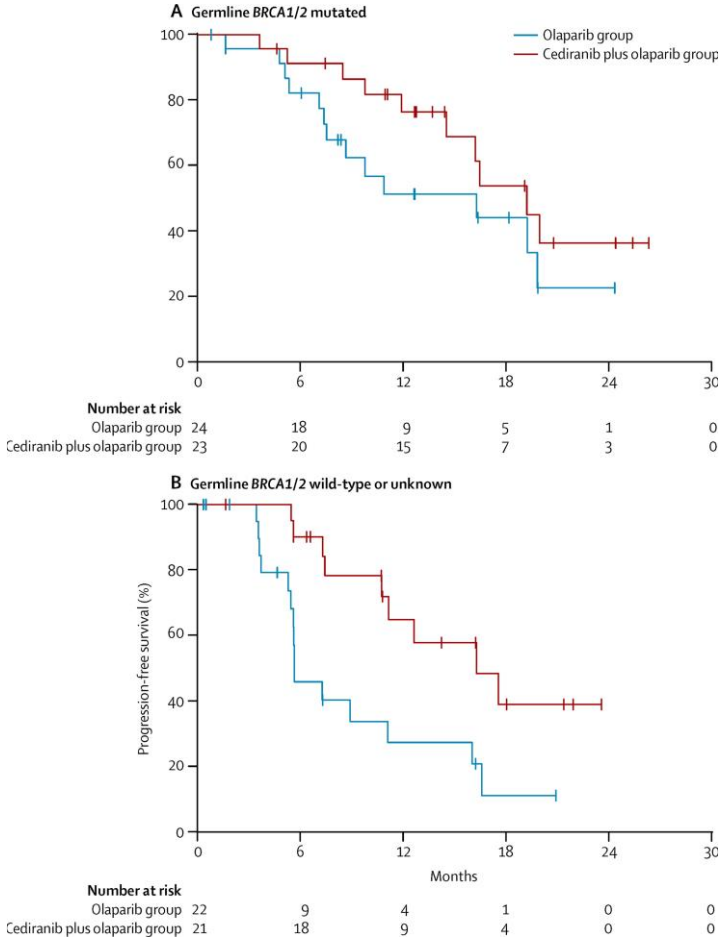

Liu et al Lancet Oncol 2014

# Cediranib/olaparib *versus* olaparib - Progression-Free survival




Liu et al Lancet Oncol 2014

# Cediranib/olaparib in BRCA mutation carriers




| PFS | BRCA Mutation Carrier | |
|---|---|---|
| | Olaparib | Cediranib/Olaparib |
| events | 13 | 10 |
| median | 16.5 mo | 19.4 mo |
| | p=0.16 | |
| | HR 0.55 (95% CI: 0.24-1.27) | |

| PFS | BRCA Non-carrier/Unknown | |
|---|---|---|
| | Olaparib | Cediranib/Olaparib |
| events | 15 | 9 |
| median | 5.7 mo | 16.5 mo |
| | p=0.008 | |
| | HR 0.32 (95% CI: 0.14-0.74) | |

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# Olaparib and PD1 Checkpoint inhibitor- Durvalumab

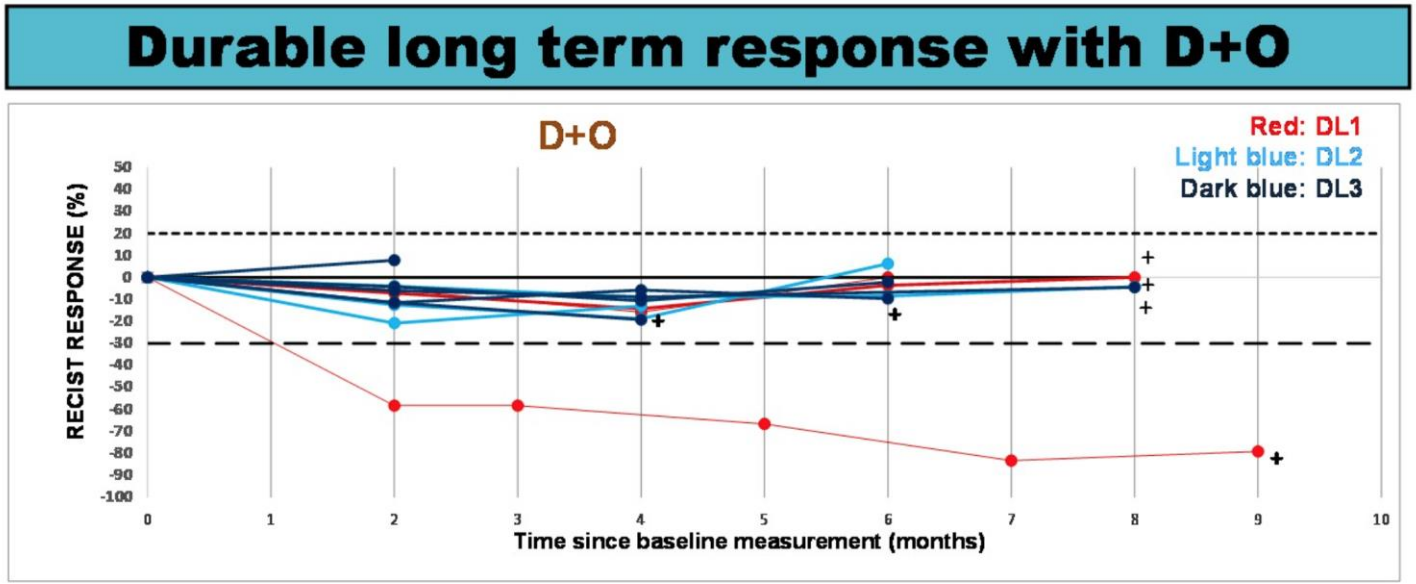


Figure 1. RECIST Response Spidergram of D+O. A majority of pts had durable response with D+O and 1 BRCA wild type OvCa pt (DL1) had PR. 6 pts are still on treatment (+).

Lee Jung-min et al ASCO 2016

# Trials combining PARP inhibitors with anti-angiogenic drugs

- Maintenance Combinations
  - **PAOLA 1** (olaparib/bevacizumab) first line
  - **ICON9** cediranib/olaparib v olaparib
- Olaparib, combinations versus chemotherapy
  - **NRG-GYN 004** olaparib+ cediranib v platinum-based chemotherapy
- Niraparib + bevacizumab
  - **AVANOVA** niraparib + bevacizumab in platinum sensitive ovarian cancer

# PARP inhibitors – a change in practice for treating ovarian cancer

- **Olaparib** is the first licensed PARP inhibitor directed at a genotypically defined predictive marker (BRCA mutation) in recurrent ovarian cancer
- Significant improvement in PFS with maintenance therapy using **olaparib or niraparib** in platinum-sensitive high-grade serous carcinoma
- **Niraparib** (FDA approved) as maintenance for all groups platinum-sensitive relapse responding to platinum-based therapy
- 15% patients on olaparib with a $BRCA^{mut}$ remain on olaparib for > 5 years
- PARP inhibitors are well-tolerated oral medications- low drop-out rate due to side effects
- Single agent therapy - **olaparib and rucaparib** approved in USA for BRCA mutated ovarian cancer- Choices maintenance versus single agent?
- Results of first-line studies awaited
- Second generation studies combining PARP inhibitors with anti-angiogenic drugs or immune checkpoint inhibitors in progress