# Emerging Opportunities in Newly Diagnosed Advanced Ovarian Cancer

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GOG Highlight Reel

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# Financial Disclosures

I have the following financial relationships to report over the past 24 months:

- *Duke receives Clinical trial grant funding from AbbVie, Aravive, AstraZeneca, Clovis, Eisai, Ellipses Pharma, GSK, I-MAB Biopharma, Immunogen, Merck, Oncoquest, Roche/Genentech, Seagen, Inc, Theradex, VBL, and the National Cancer Trial Network.*

- *Participation on Steering Committees (uncompensated): Aravive (AxXelerate); Roche/Genentech (AtTEND trial); VBL (OVAL trial); and Oncoquest (GOG-3035/FLORA-5).*

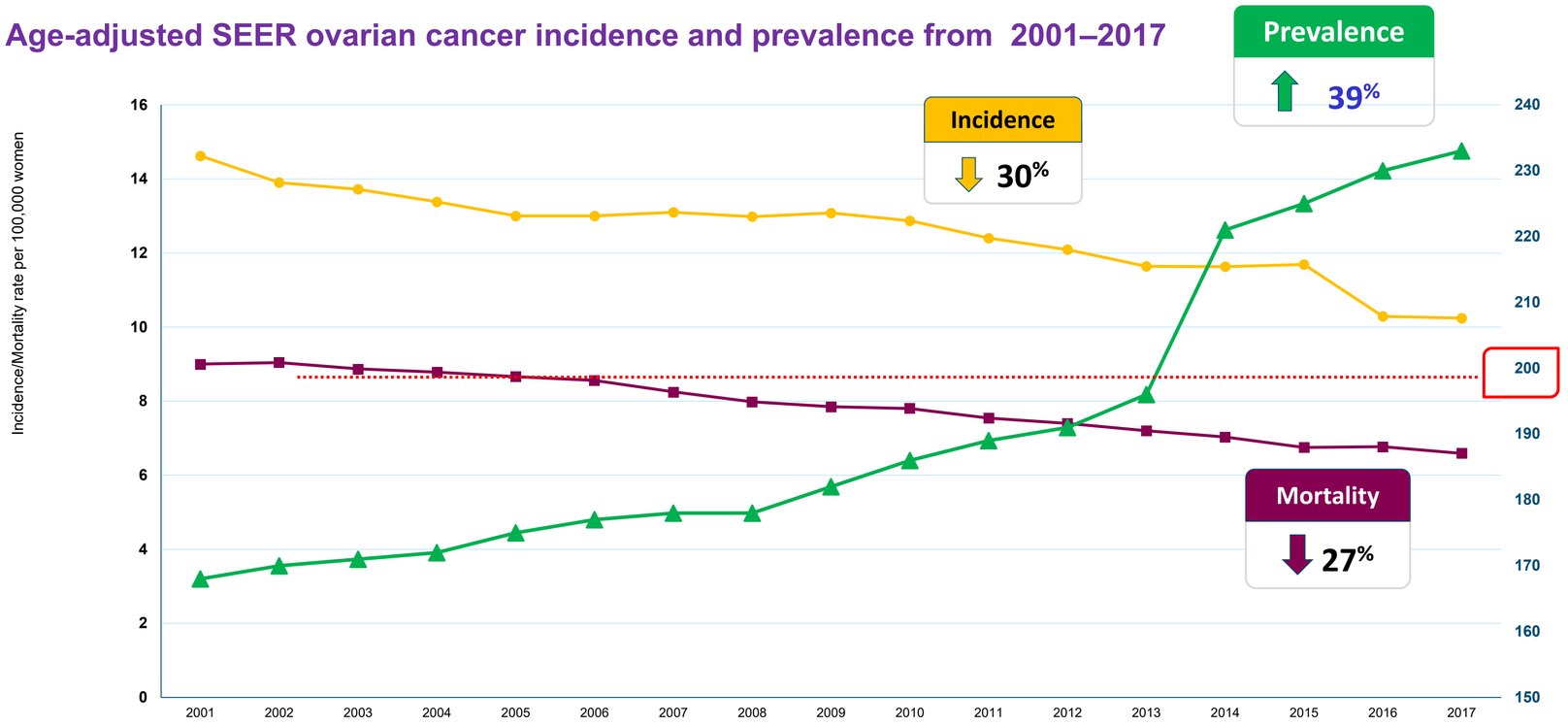
- *SGO Board of Directors, GOG Foundation Board of Directors, AAOGF Board of Trustees*

# Objectives

- *Review updated survival data from front-line ovarian cancer PARPi maintenance therapy trials*
  - *SOLO-1/GOG 3004, PAOLA-1, and PRIMA/GOG 3012*
- *Review HIPEC trials*
- *Discuss context of these findings and identify gaps in care.*
- *Highlight ongoing GOG-F front-line trials*
  - *FLORA-5/GOG 3035*
  - *HOTT*

# Ovarian Cancer: Clinical Impact

## Age-adjusted SEER ovarian cancer incidence and prevalence from 2001–2017




**SEER=Surveillance, Epidemiology and End Results.**

**National Cancer Institute Surveillance, Epidemiology and End Results Program (SEER). SEER Cancer Statistics Review (CSR) 1975-2016 - Ovary. 2016; https://seer.cancer.gov/csr/1975_2016/sections.html. Accessed Apr 14, 2020.**

**10-year survival is ~ 17%**

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# SOLO1/GOG 3004: Updated overall survival at 7-year follow up for newly diagnosed advanced ovarian cancer patients with a *BRCA* mutation

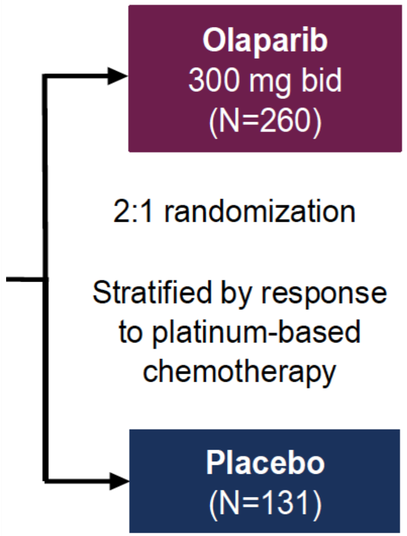
-Newly diagnosed stage III-IV, high-grade serous or endometrioid ovarian, tubal, or peritoneal cancer

-*BRCA* mutation

-ECOG PS 0-1

-Cytoreductive surgery*

-In clinical CR^ or PR after platinum-based therapy




**For up to 2 years until disease progression**

**Primary endpoint:**
**PFS – IA**

**Secondary endpoints:**
**OS**
**TFST**
**TSST**
**Safety**

**Primary PFS analysis[1] (DCO 17 May 2018)**

| | Olaparib (N=260) | Placebo (N=131) |
|---|---|---|
| **Events,** n (%) | 102 (39.2) | 96 (73.3) |
| **Median PFS,** months | NR | 13.8 |
| **3-year PFS rate,** % | 60.4 | 26.9 |
| | **HR 0.30** (95% CI 0.23–0.41) | |
| | *P*<0.001 | |

**Updated PFS analysis[2] (DCO 5 March 2020)**

| | Olaparib (N=260) | Placebo (N=131) |
|---|---|---|
| **Events,** n (%) | 118 (45.4) | 100 (76.3) |
| **Median PFS,** months | 56.0 | 13.8 |
| **5-year PFS rate,** % | 48.3 | 20.5 |
| | **HR 0.33** (95% CI 0.25–0.43) | |

***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**
**^Including patients with no evidence of disease**

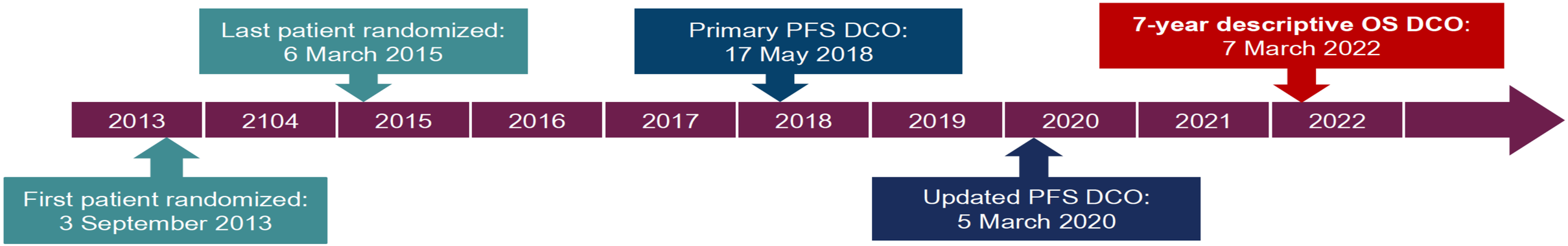


**Moore, K *et al N Engl J Med* 2018; Banerjee S *et al Lancet Oncol* 2021**

# SOLO1/GOG 3004:
# Updated Overall Survival Analysis

## Statistical Analysis

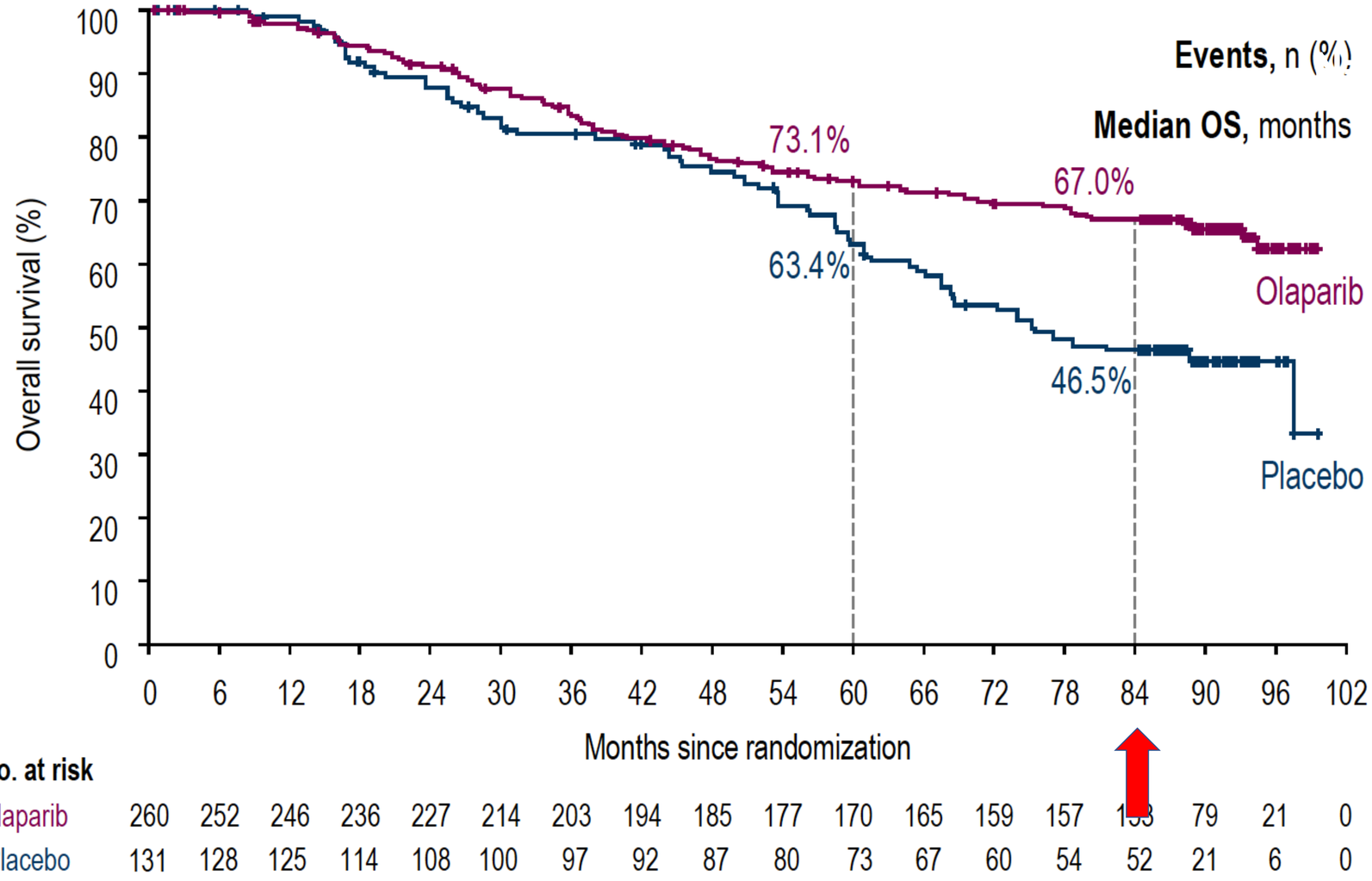
- Prespecified descriptive OS analysis conducted at 7 years after last patient randomized
  - OS unadjusted for subsequent PARPi therapy
- Two-sided P value of <0.0001 required to declare statistical significance
- Prespecified final OS analysis currently planned to be conducted at approximately 60% data maturity



# SOLO1/GOG 3004:
# Updated Overall Survival Analysis Patients Disposition

| | Olaparib | Placebo |
|---|---|---|
| **Completed treatment at 2 years per protocol, n (%)** | 123 (47.3) | 35 (26.9) |
| **Continued treatment beyond 2 years,* n (%)** | 26 (10.0) | 3 (2.3) |
| **Still receiving treatment at DCO, n (%)** | 7 (2.7) | 0 |
| **Discontinued treatment for reasons other than completing the prescribed regimen, n (%)** | 130 (50.0) | 95 (73.1) |
| Objective disease progression | 53 (20.4) | 78 (60.0) |
| Adverse event | 31 (11.9) | 3 (2.3) |
| Patient decision | 23 (8.8) | 2 (1.5) |
| Other†/unknown reason | 23 (8.8) | 12 (9.2) |
| **Median (range) duration of treatment, months** | 24.6 (0.0–97.5) | 13.9 (0.2–60.9) |
| **Median (IQR) duration of follow-up for OS, months** | 88.9 (85.7–93.6) | 87.4 (84.3–91.7) |

# SOLO1/GOG 3004:
# Updated Overall Survival Analysis Overall Survival




| Olaparib (N=260) | Placebo (N=131) |
|---|---|
| 84 (32.3) | 65 (49.6) |
| NR | 75.2 |

**HR 0.55** (95% CI 0.40–0.76); *P*=0.0004*

***P* < 0.0001 required to declare statistical significance**

**44.3% patients in placebo arm received subsequent PARPi, compared to 14.6% of patients in the olaparib group**

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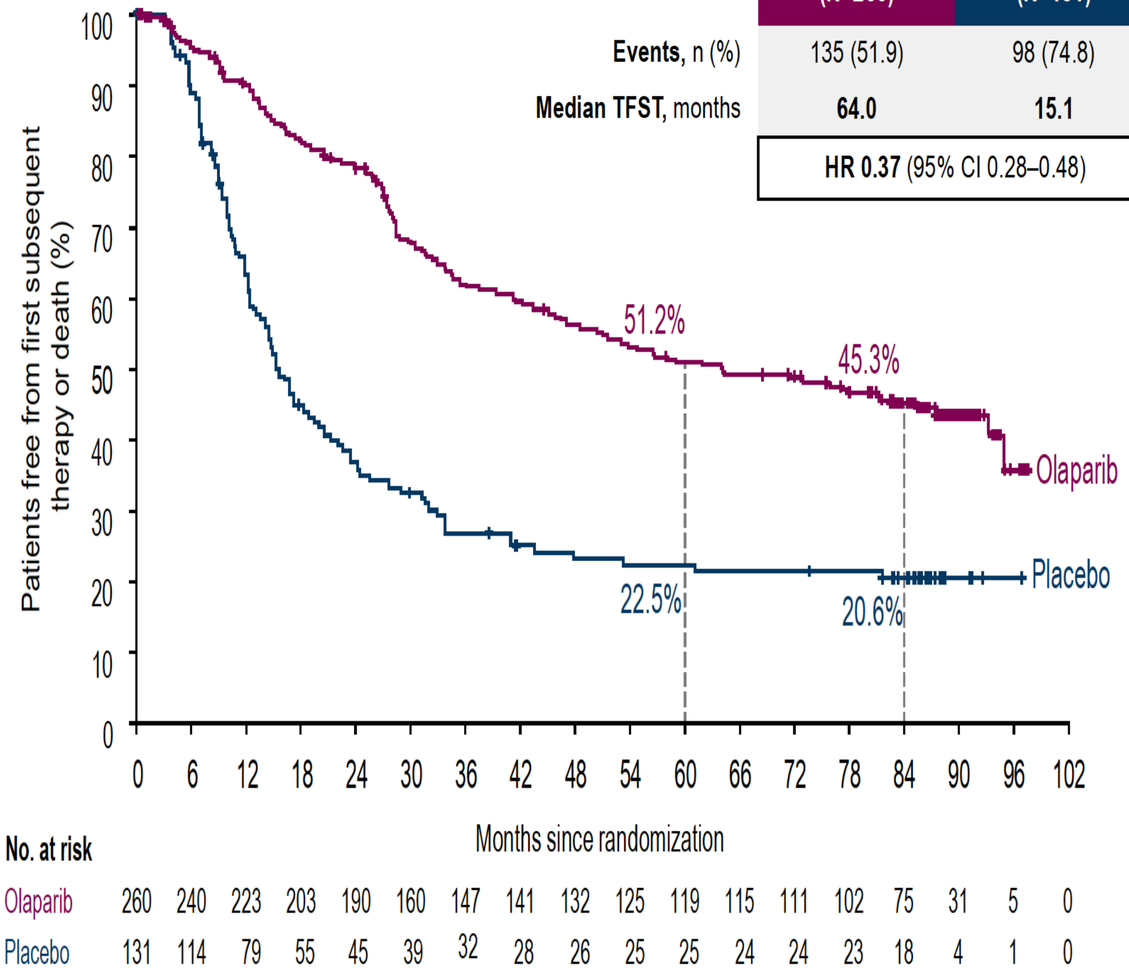
# SOLO1/GOG 3004:
# Updated Overall Survival Analysis TFST and TSST

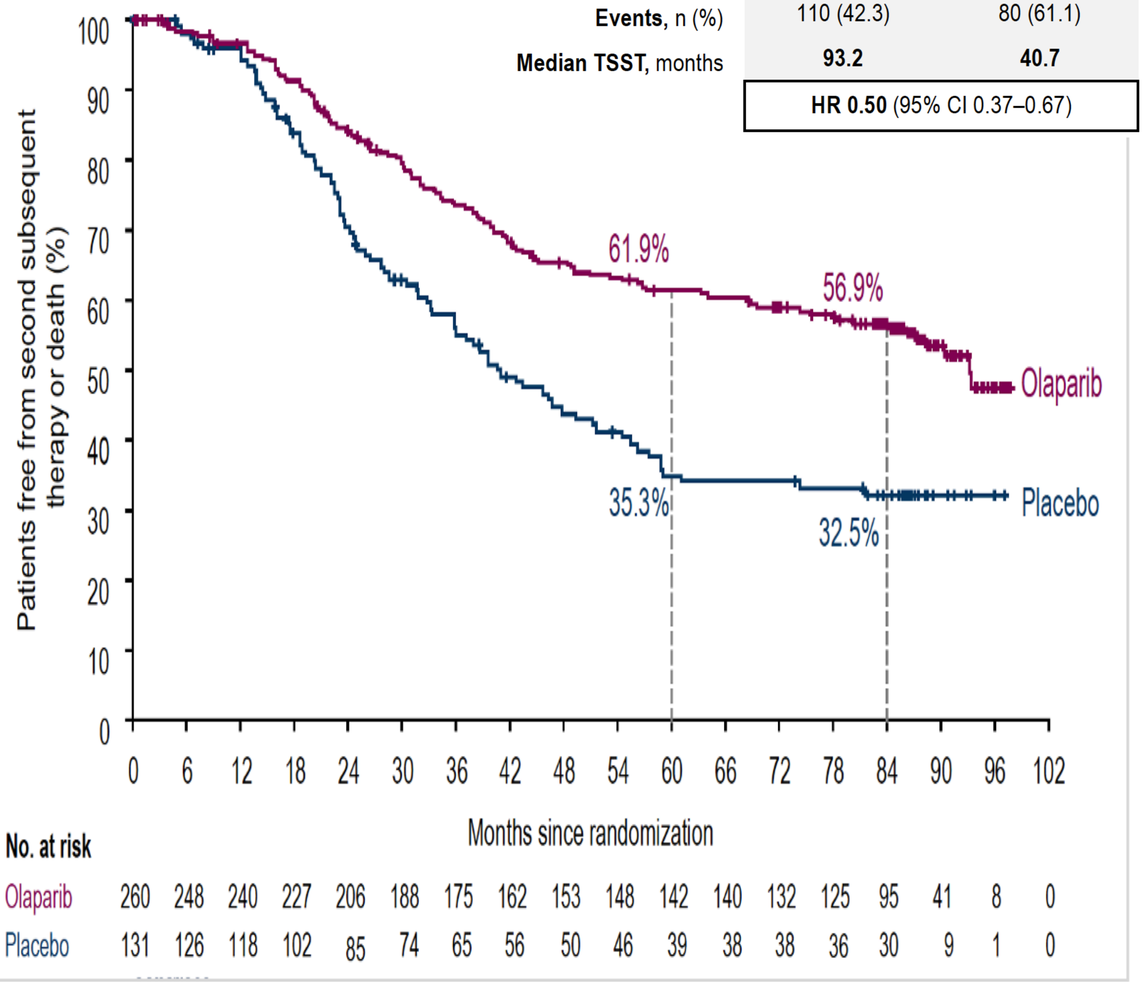
| | Olaparib (N=260) | Placebo (N=131) |
|---|---|---|
| **Events**, n (%) | 135 (51.9) | 98 (74.8) |
| **Median TFST**, months | **64.0** | **15.1** |
| **HR 0.37** (95% CI 0.28–0.48) | | |




**No. at risk**

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Olaparib | 260 | 240 | 223 | 203 | 190 | 160 | 147 | 141 | 132 | 125 | 119 | 115 | 111 | 102 | 75 | 31 | 5 | 0 |
| Placebo | 131 | 114 | 79 | 55 | 45 | 39 | 32 | 28 | 26 | 25 | 25 | 24 | 24 | 23 | 18 | 4 | 1 | 0 |

| | Olaparib (N=260) | Placebo (N=131) |
|---|---|---|
| **Events**, n (%) | 110 (42.3) | 80 (61.1) |
| **Median TSST**, months | **93.2** | **40.7** |
| **HR 0.50** (95% CI 0.37–0.67) | | |




**No. at risk**

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Olaparib | 260 | 248 | 240 | 227 | 206 | 188 | 175 | 162 | 153 | 148 | 142 | 140 | 132 | 125 | 95 | 41 | 8 | 0 |
| Placebo | 131 | 126 | 118 | 102 | 85 | 74 | 65 | 56 | 50 | 46 | 39 | 38 | 38 | 36 | 30 | 9 | 1 | 0 |

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# SOLO1/GOG 3004:
# Updated Overall Survival Analysis Safety

| | Primary PFS analysis (DCO 17 May 2018) | | 7-year descriptive OS analysis (DCO 7 March 2022) | |
|---|---|---|---|---|
| | Olaparib (N=260) | Placebo (N=130) | Olaparib (N=260) | Placebo (N=130) |
| Median (range) duration of treatment, months | 24.6 (0.0–52.0) | 13.9 (0.2–45.5) | 24.6 (0.0–97.5) | 13.9 (0.2–60.9) |
| Any TEAE, n (%) | 256 (98.5) | 120 (92.3) | 256 (98.5) | 120 (92.3) |
| Grade ≥3 TEAEs, n (%) | 102 (39.2) | 24 (18.5) | 103 (39.6) | 26 (20.0) |
| Serious TEAEs, n (%) | 54 (20.8) | 16 (12.3) | 55 (21.2) | 18 (13.8) |
| TEAE leading to dose interruption, n (%) | 135 (51.9) | 22 (16.9) | 137 (52.7) | 22 (16.9) |
| TEAE leading to dose reduction, n (%) | 74 (28.5) | 4 (3.1) | 75 (28.8) | 4 (3.1) |
| TEAE leading to treatment discontinuation, n (%) | 30 (11.5) | 3 (2.3) | 31 (11.9) | 4 (3.1) |
| AEs of special interest, n (%) | | | | |
| MDS/AML* | 3 (1.2) | 0 | 4 (1.5) | 1 (0.8) |
| New primary malignancies* | 5 (1.9) | 3 (2.3) | 14 (5.4)† | 8 (6.2)‡ |
| Pneumonitis/ILD | 5 (1.9) | 0 | 5 (1.9) | 0 |

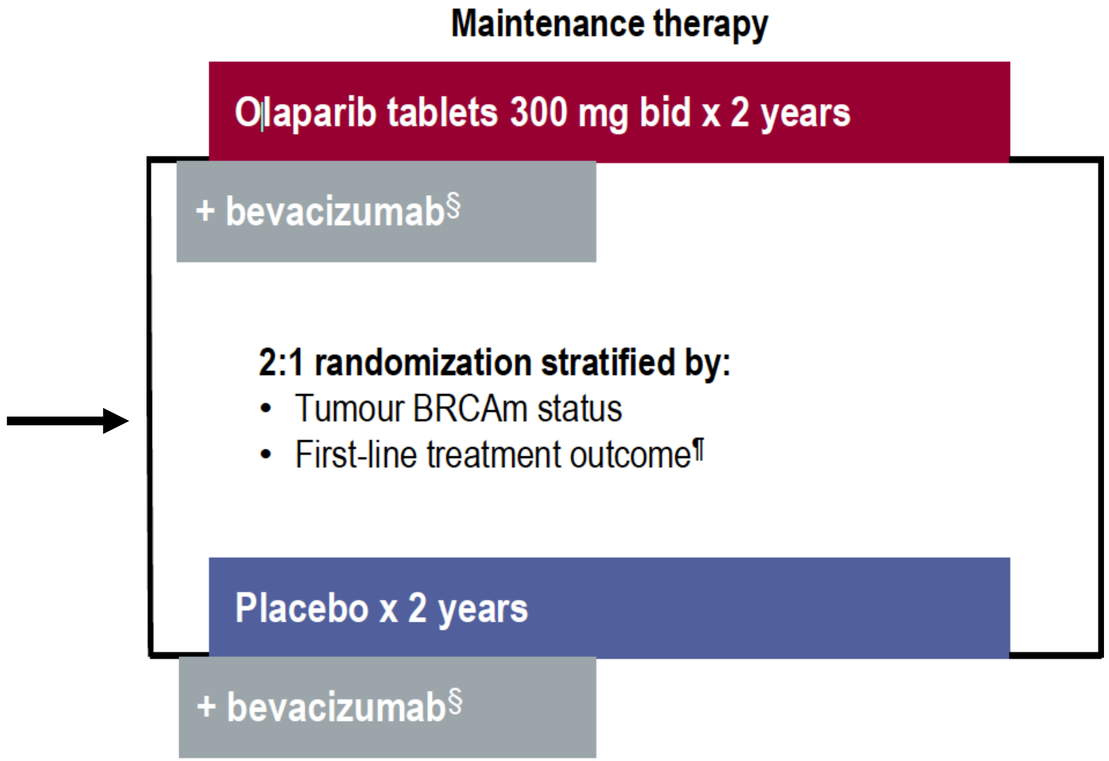
# PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

-Newly diagnosed stage III-IV, high-grade serous or endometrioid ovarian, tubal, or peritoneal cancer*

-Upfront or interval Cytoreductive surgery

-Platinum-taxane based therapy plus ≥ 2 cycles of bevacizumab

-NED/CR/PR




Primary endpoint:
PFS – IA

Secondary endpoints:
PFS2
OS

*OS planned for 3 years after the primary PFS analysis or 60% of data maturity

*Patients with other epithelial non-mucinous ovarian cancer eligible if *BRCA*m present.

OS will be tested at full 5% alpha at OS data cufoff
Predefined OS subgroup analysis by tumor *BRCA*m and HRD score

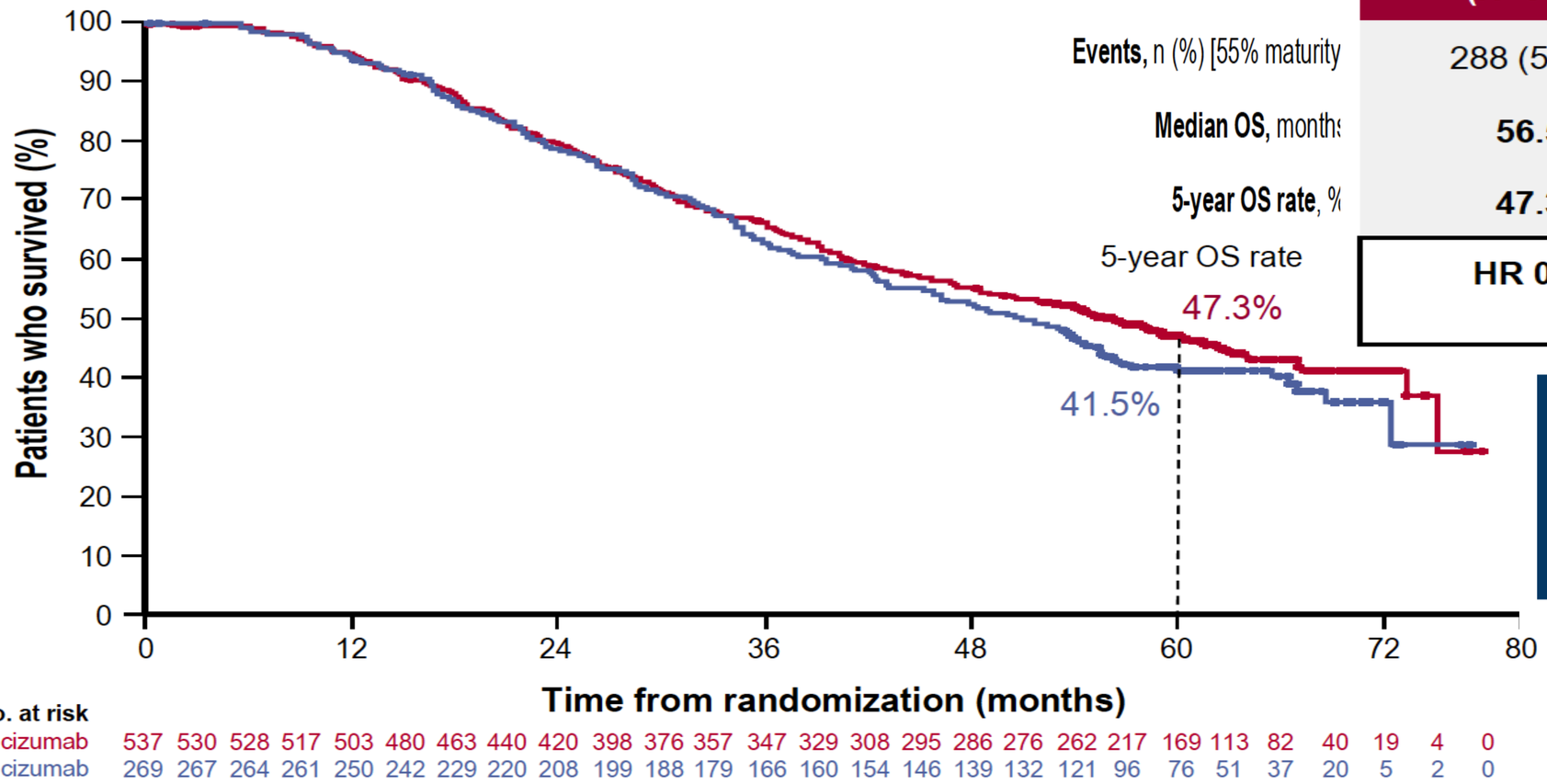
# PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

## Patient Characteristics

| | | Olaparib + bevacizumab (N=537) | Placebo + bevacizumab (N=269) |
|---|---|---|---|
| **Age, median, years (range)** | | 61 (32–87) | 60 (26–85) |
| **FIGO stage, n (%)** | III | 378 (70) | 186 (69) |
| | IV | 159 (30) | 83 (31) |
| **HRD status,* n (%)** | HRD positive | 255 (47) | 132 (49) |
| | tBRCAm | 157 (29) | 80 (30) |
| | HRD positive excluding tBRCAm | 97 (18) | 55 (20) |
| | HRD negative/HRD unknown | 282 (53) | 137 (51) |
| | HRD negative | 192 (36) | 85 (32) |
| **History of cytoreductive surgery, n (%)** | Upfront surgery | 271 (50) | 138 (51) |
| | • No residual macroscopic disease | 160 (59) | 85 (62) |
| | • Residual macroscopic disease | 111 (41) | 53 (38) |
| | Interval cytoreductive surgery | 228 (42) | 110 (41) |
| | • No residual macroscopic disease | 163 (71) | 75 (68) |
| | • Residual macroscopic disease | 65 (29) | 35 (32) |
| | No surgery | 38 (7) | 21 (8) |
| **Response after surgery/PBC, n (%)** | NED | 290 (54) | 141 (52) |
| | CR | 106 (20) | 53 (20) |
| | PR | 141 (26) | 75 (28) |

# PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

## Overall Survival ITT Population




| | Olaparib + bevacizumab (N=537) | Placebo + bevacizumab (N=269) |
|---|---|---|
| **Events**, n (%) [55% maturity | 288 (53.6) | 158 (58.7) |
| **Median OS**, months | **56.5** | **51.6** |
| **5-year OS rate**, % | **47.3** | **41.5** |

**HR 0.92** (95% CI 0.76–1.12); ***P*=0.4118**

**Patients receiving a PARP inhibitor during any subsequent treatment**
Olaparib + bevacizumab: **19.6%** (105/537)
Placebo + bevacizumab: **45.7%** (123/269)



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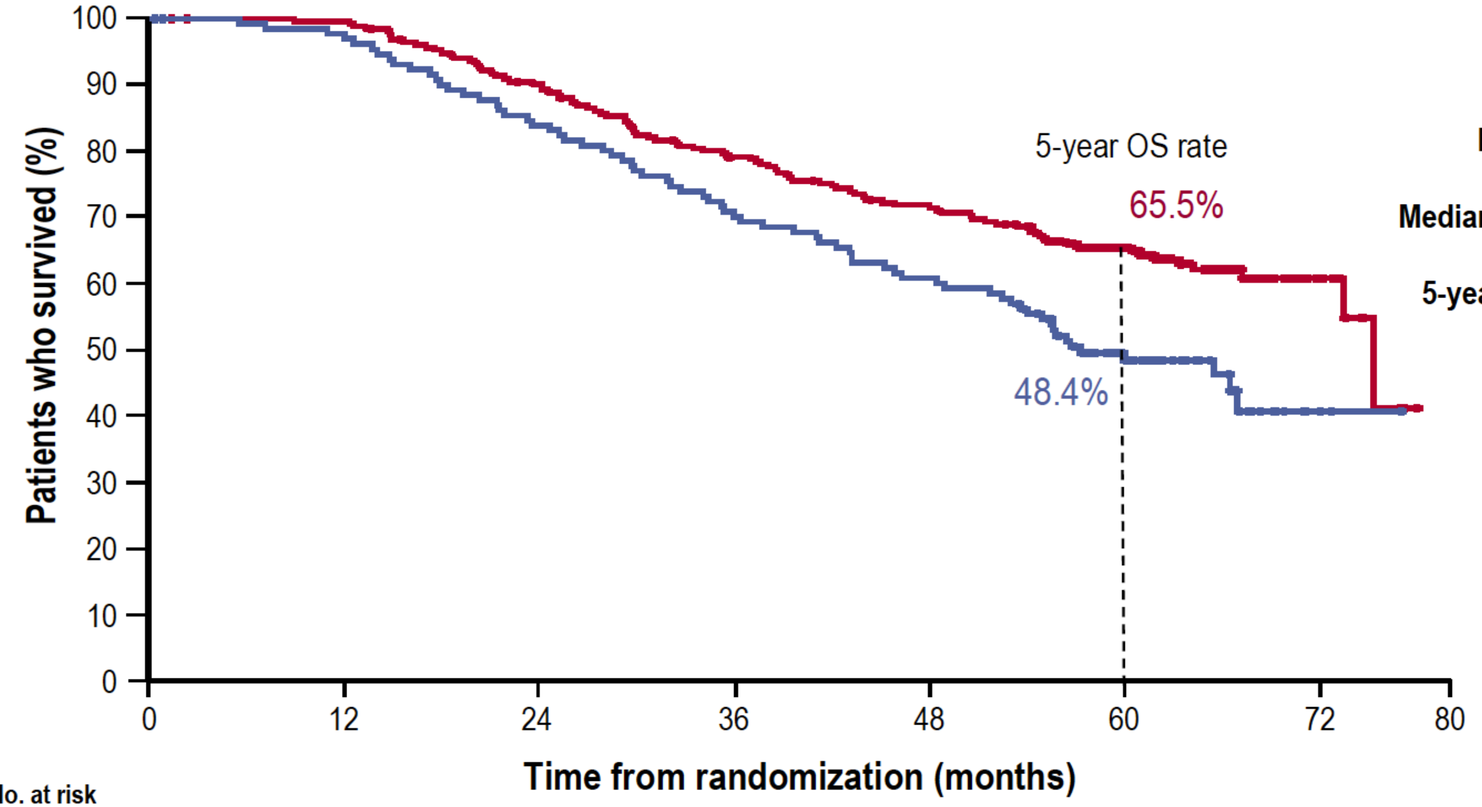
# PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

## Overall Survival HRD Population




| No. at risk | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Olaparib + bevacizumab | 255 | 253 | 253 | 252 | 252 | 244 | 238 | 231 | 225 | 215 | 205 | 200 | 195 | 189 | 183 | 176 | 174 | 170 | 164 | 142 | 116 | 83 | 62 | 32 | 17 | 4 | 0 |
| Placebo + bevacizumab | 132 | 130 | 129 | 128 | 126 | 121 | 117 | 114 | 109 | 105 | 100 | 96 | 91 | 89 | 86 | 82 | 79 | 77 | 70 | 59 | 44 | 29 | 21 | 9 | 2 | 1 | 0 |

| | Olaparib + bevacizumab (N=255) | Placebo + bevacizumab (N=132) |
|---|---|---|
| **Events**, n (%) | 93 (36.5) | 69 (52.3) |
| **Median OS**, months | **75.2** (unstable)* | **57.3** |
| **5-year OS rate**, % | **65.5** | **48.4** |

**HR 0.62** (95% CI 0.45–0.85)

38% reduction in risk of death for olaparib + bevacizumab vs bevacizumab alone

**Patients receiving a PARP inhibitor during any subsequent treatment**
Olaparib + bevacizumab: **17.3%** (44/255)
Placebo + bevacizumab: **50.8%** (67/132)

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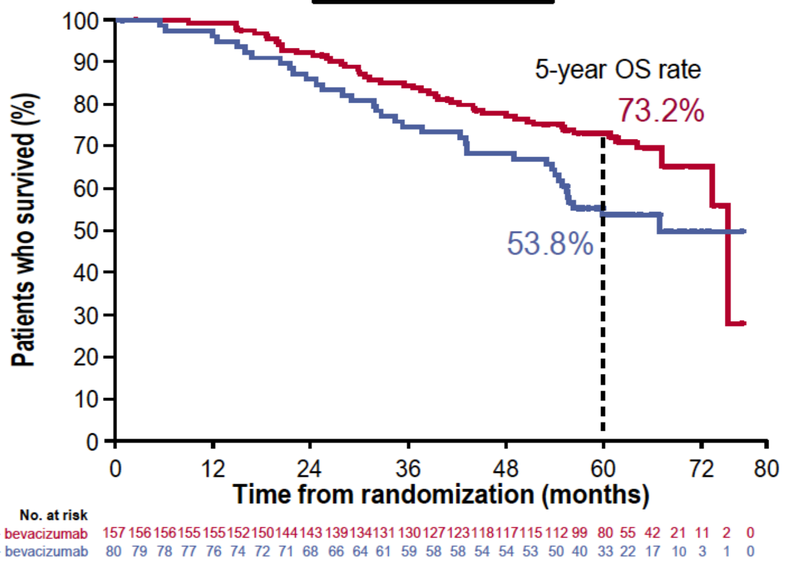
# PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

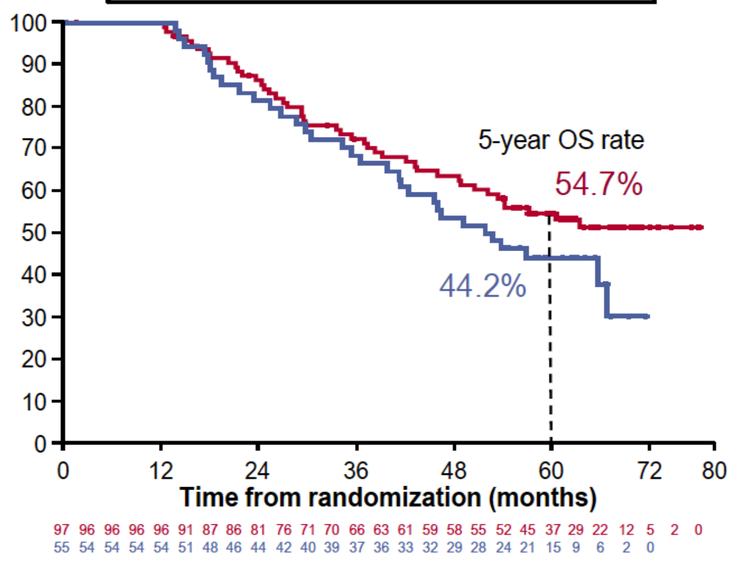
## Overall Survival Subgroup Analysis *BRCA*m and HRD Status

### BRCAm*



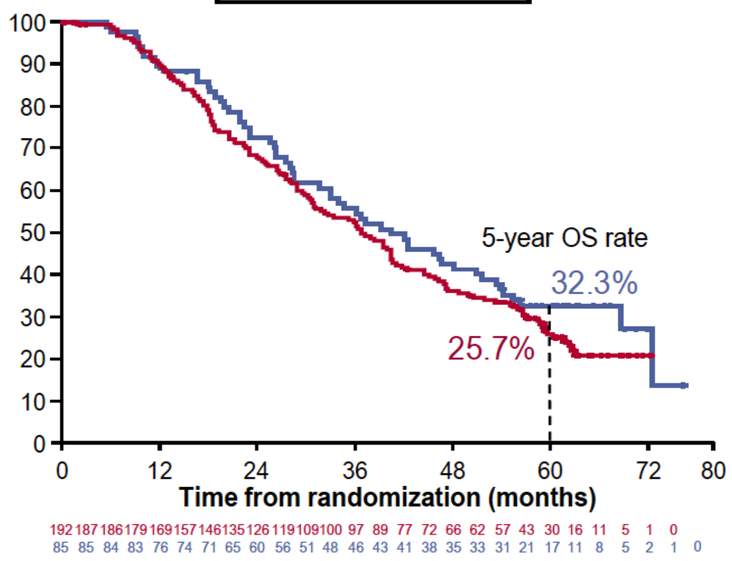

| | Olaparib + bevacizumab (N=157) | Placebo + bevacizumab (N=80) |
|---|---|---|
| **Events**, n (%) | 48 (30.6) | 37 (46.3) |
| **Median OS**, months | 75.2 (unstable)† | 66.9 |
| **5-year OS rate**, % | **73.2** | **53.8** |
| **PARPi as subsequent treatment, n (%)** | 38 (24.2) | 44 (55.0) |
| | **HR 0.60** (95% CI 0.39–0.93) | |

### HRD positive‡ excluding BRCAm




| | Olaparib + bevacizumab (N=97) | Placebo + bevacizumab (N=55) |
|---|---|---|
| | 44 (45.4) | 32 (58.2) |
| | NR | 52.0 |
| | **54.7** | **44.2** |
| | 9 (9.3) | 23 (41.8) |
| | **HR 0.71** (95% CI 0.45–1.13) | |

### HRD negative†




| | Olaparib + bevacizumab (N=192) | Placebo + bevacizumab (N=85) |
|---|---|---|
| | 140 (72.9) | 58 (68.2) |
| | 36.8 | 40.4 |
| | **25.7** | **32.3** |
| | 46 (24.0) | 34 (40.0) |
| | **HR 1.19** (95% CI 0.88–1.63) | |

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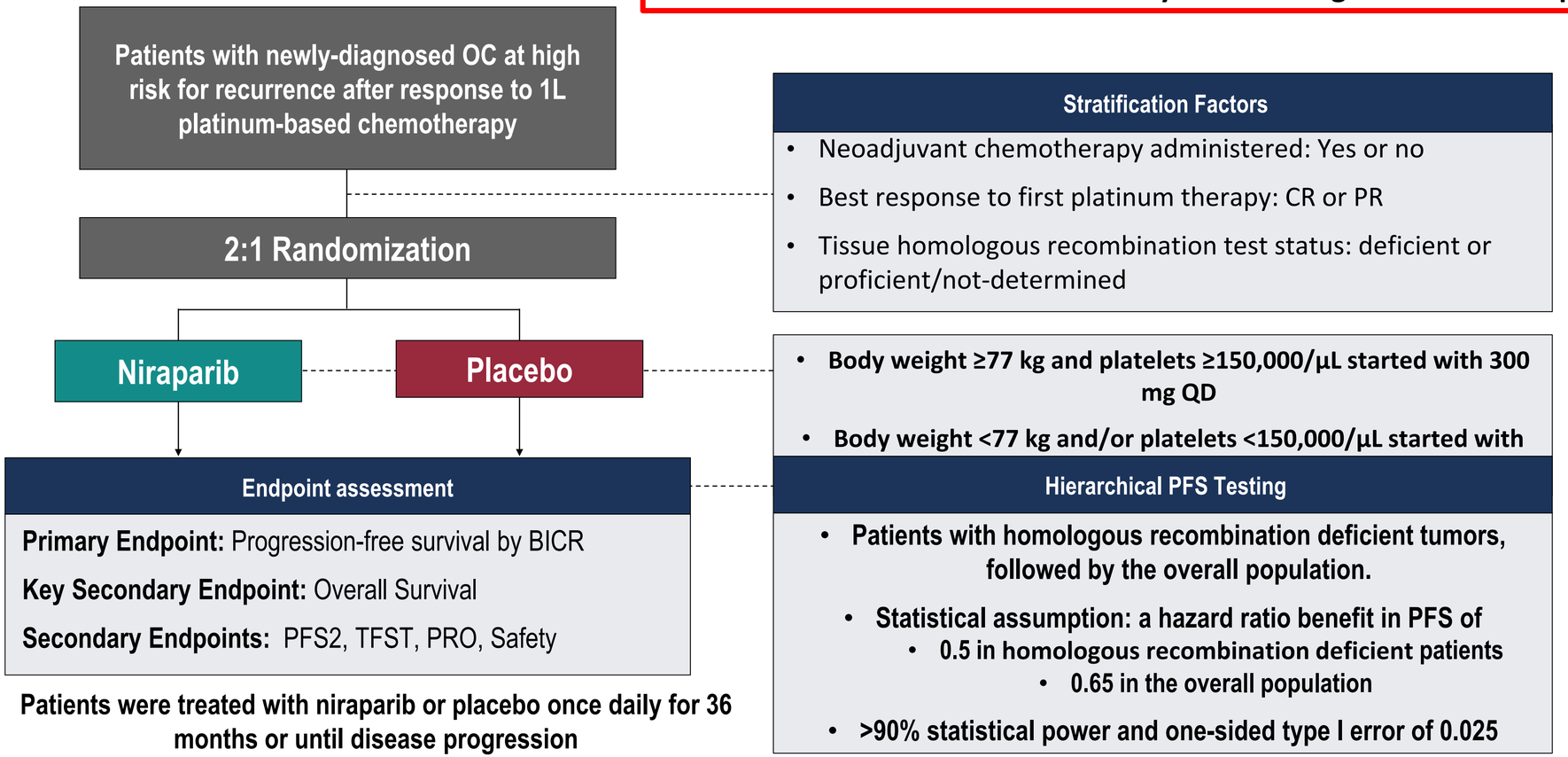
# PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

## Adverse Events of Special Interest

| | Primary PFS analysis (DCO: 22 March 2019) | | Final PFS2 analysis (DCO: 22 March 2020) | | Final OS analysis (DCO: 22 March 2022) | |
|---|---|---|---|---|---|---|
| | Olaparib + bevacizumab (N=535) | Placebo + bevacizumab (N=267) | Olaparib + bevacizumab (N=535) | Placebo + bevacizumab (N=267) | Olaparib + bevacizumab (N=535) | Placebo + bevacizumab (N=267) |
| MDS/AML/AA, n (%) | 6 (1.1) | 1 (0.4) | 7 (1.3) | 4 (1.5) | 9 (1.7) | 6 (2.2) |
| New primary malignancies, n (%)* | 7 (1.3) | 3 (1.1) | 13 (2.4) | 5 (1.9) | 22 (4.1) | 8 (3.0) |
| Pneumonitis/ILD/bronchiolitis, n (%)† | 6 (1.1) | 0 (0.0) | 6 (1.1) | 0 (0.0) | 7 (1.3) | 2 (0.7) |

# PRIMA/GOG 3012/ENGOT-ov26: Updated long-term PFS and safety

***Excluded stage III no visible residual after CRS and BEV maintenance.**
**Residual tumour after CT ≤ 2 cm**
**Normal CA125 or CA125 decrease by >90% during front-line therapy**




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

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 subsequent therapy.

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**OS remains immature – 41.2% of overall population**
**Subsequent PARPi therapy: 9.2% niraparib group vs 33.3% placebo-group**

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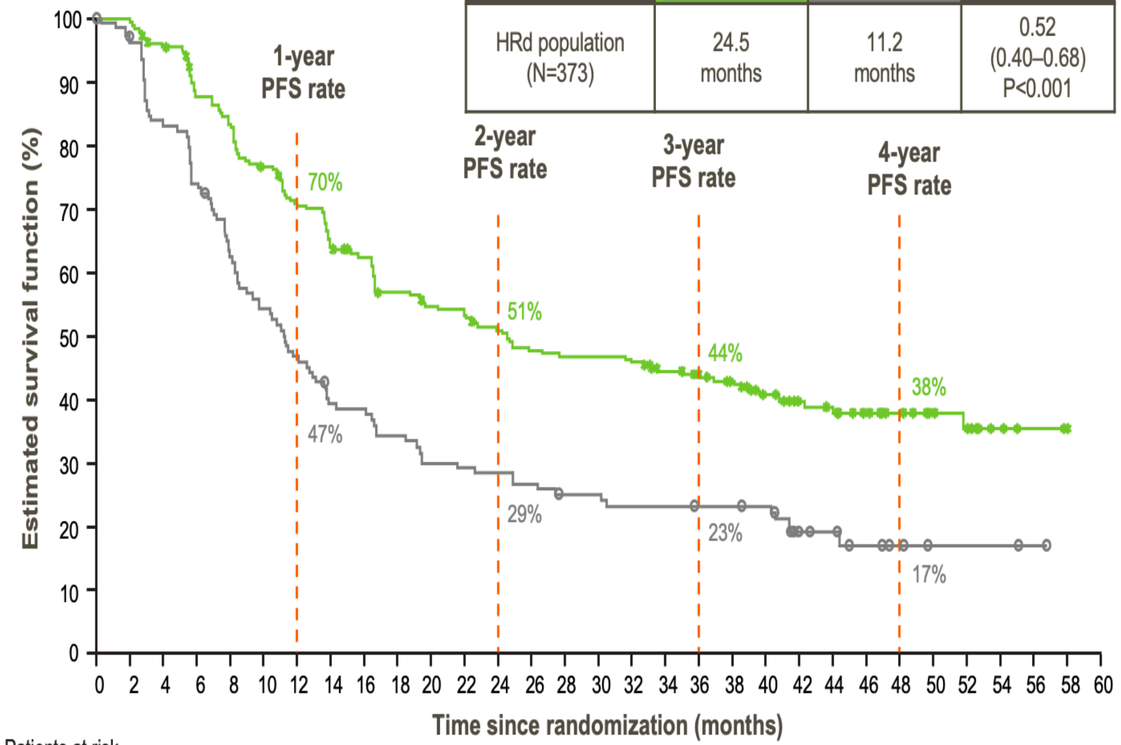
# PRIMA/GOG-3012/ENGOT-ov26: Updated long-term PFS

## HRD and Overall Population

### HRD

| Population | Niraparib mPFS | Placebo mPFS | Hazard ratio (95% CI) |
|---|---|---|---|
| HRd population (N=373) | 24.5 months | 11.2 months | 0.52 (0.40–0.68) P<0.001 |

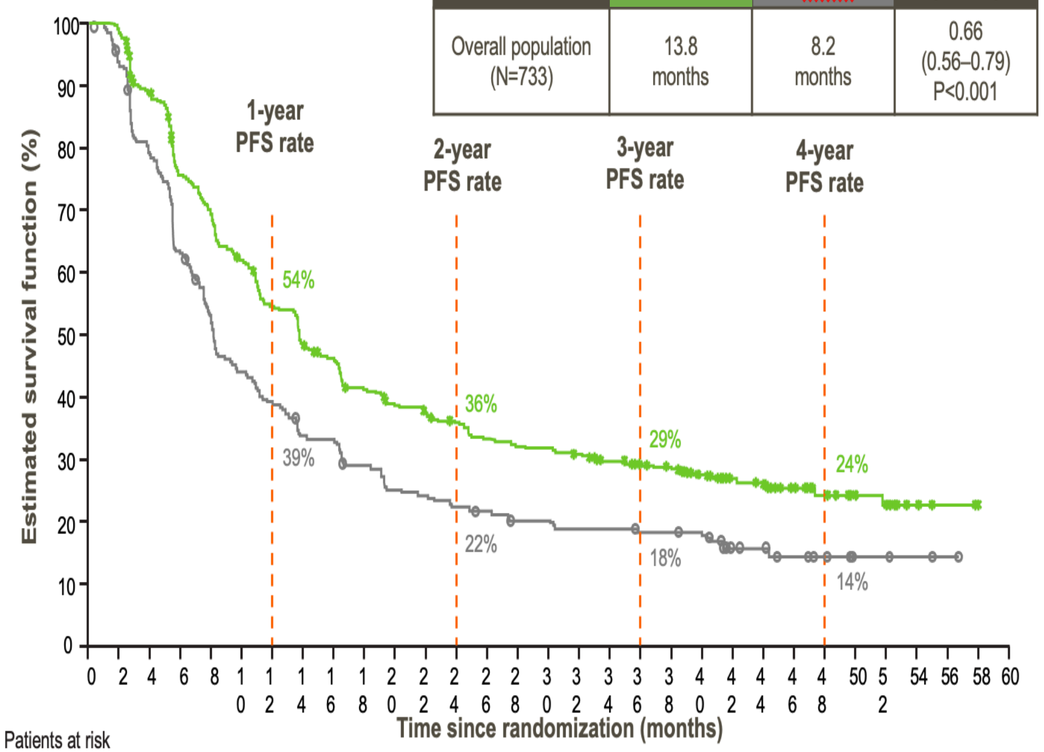



Patients at risk

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Zejula | 247 | 236 | 222 | 200 | 190 | 174 | 159 | 144 | 138 | 125 | 119 | 116 | 110 | 103 | 101 | 101 | 99 | 92 | 87 | 82 | 71 | 48 | 45 | 38 | 21 | 17 | 15 | 4 | 2 | 1 | 0 |
| Placebo | 126 | 118 | 102 | 91 | 76 | 66 | 57 | 47 | 46 | 41 | 36 | 35 | 34 | 32 | 28 | 28 | 26 | 26 | 25 | 25 | 24 | 11 | 10 | 7 | 5 | 2 | 2 | 2 | 1 | 0 | |

### Overall

| Population | Niraparib mPFS | Placebo mPFS | Hazard ratio (95% CI) |
|---|---|---|---|
| Overall population (N=733) | 13.8 months | 8.2 months | 0.66 (0.56–0.79) P<0.001 |




Patients at risk

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Zejula | 487 | 462 | 407 | 342 | 317 | 279 | 244 | 217 | 204 | 181 | 168 | 162 | 152 | 141 | 136 | 135 | 129 | 121 | 114 | 108 | 95 | 60 | 57 | 44 | 21 | 17 | 15 | 4 | 2 | 1 | 0 |
| Placebo | 246 | 226 | 191 | 151 | 125 | 103 | 92 | 78 | 77 | 66 | 57 | 55 | 51 | 48 | 43 | 43 | 40 | 40 | 37 | 37 | 36 | 16 | 15 | 10 | 7 | 3 | 3 | 2 | 1 | 0 | |

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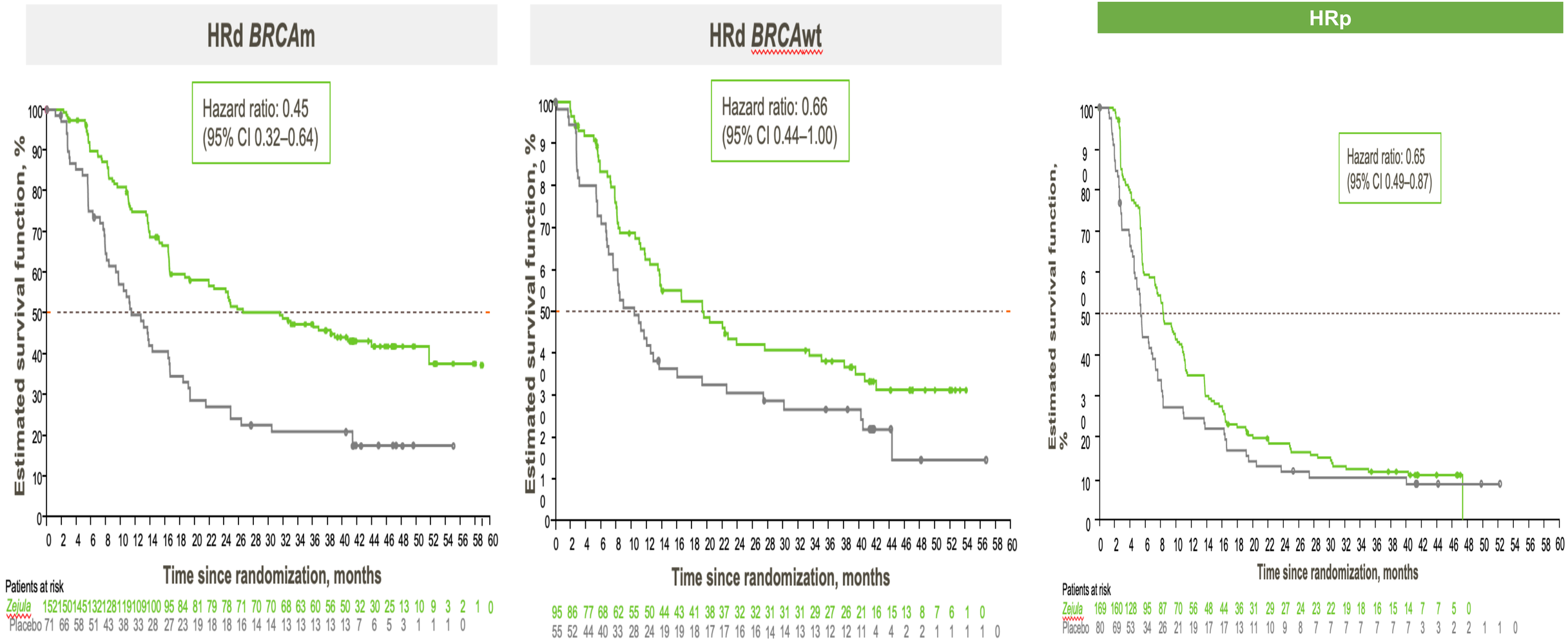
# PRIMA/GOG-3012/ENGOT-ov26: Updated long-term PFS

## HRD *BRCA*m, HRD *BRCA*wt, and HRP Subgroup Analysis

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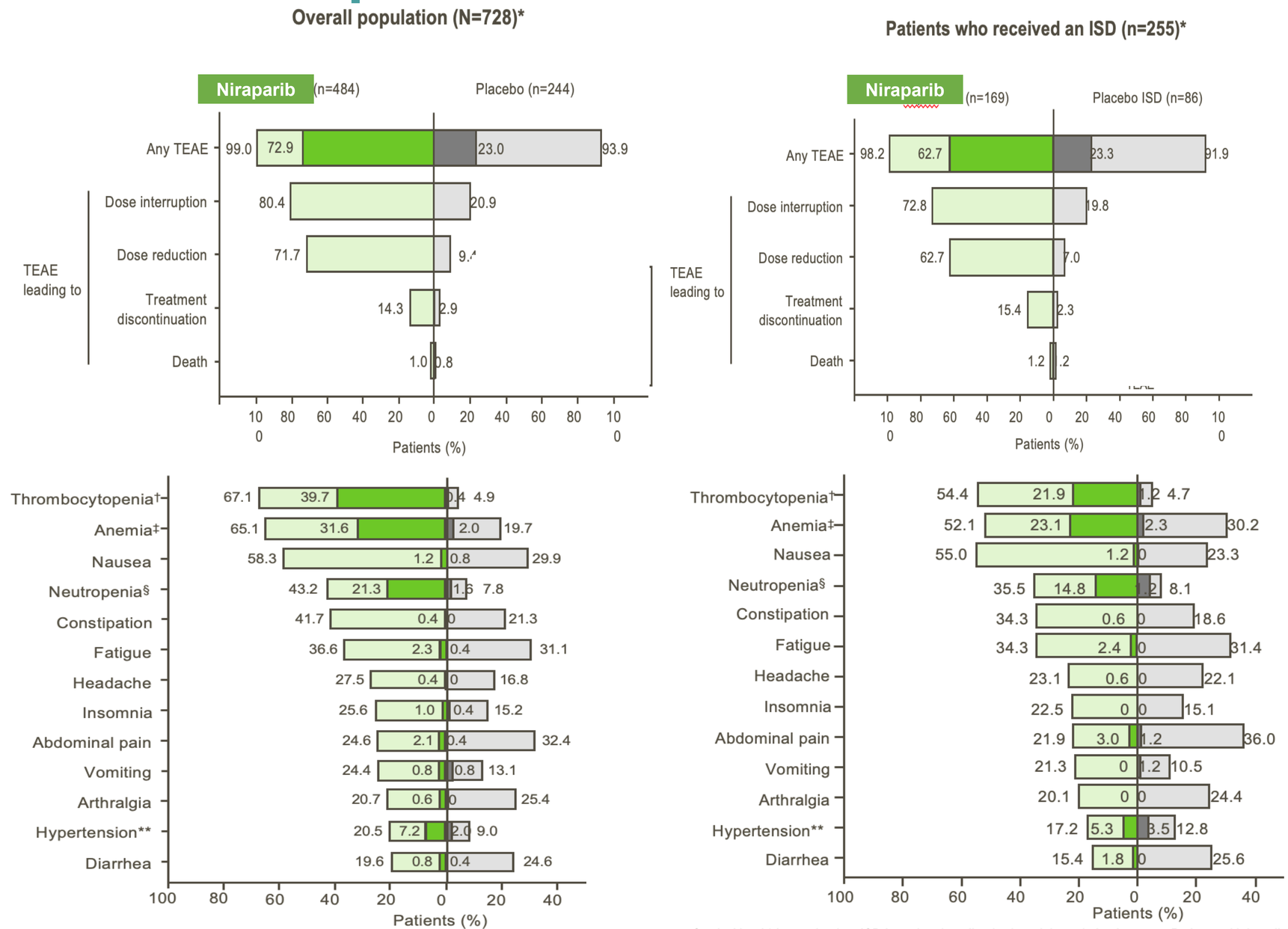
# PRIMA/GOG-3012/ENGOT-ov26: Updated long-term PFS

## Dose Interruptions and Reductions




- Niraparib any grade TEAE
- Niraparib grade ≥ 3 TEAE
- Placebo any grade TEAE
- Placebo grade ≥ 3 TEAE

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# PARPi for Frontline Maintenance Therapy: Key Efficacy Data

| Efficacy | PRIMA[1, 6] (N=733) | PRIME[2] (N=384) (study in China) | SOLO-1[3, 8] (N=391) | ATHENA-MONO[4] (N=538) | PAOLA-1[5, 7] (N=806) |
|---|---|---|---|---|---|
| Treatment | Niraparib vs placebo | Niraparib vs placebo | Olaparib vs placebo | Rucaparib vs placebo | Olaparib/Bev vs Bev |
| **PFS** | | | | | |
| ITT | 13.8 vs 8.2<br>0.66 (0.56-0.79) | 24.8 vs 8.3<br>0.45 (0.34-0.60) | - | 20.2 vs 9.2<br>0.52 (0.40-0.68) | 22.1 vs 16.6<br>0.59 (0.49-0.72) |
| *BRCA*wt/HRp | 8.1 vs 5.4*<br>0.49 (0.49-0.87) | 14.0 vs 5.5<br>0.41 (0.25-0.65) | - | 12.1 vs 9.1<br>0.65 (0.45-0.95) | 16.9 vs 16.0<br>1.00 (0.75-1.35)[b] |
| *BRCA*wt/HRd | 19.6 vs 8.2*<br>0.66 (0.44-1.00) | 24.8 vs 11.1<br>0.58 (0.36-0.93) | - | 20.3 vs 9.2<br>0.58 (0.33-1.01) | 28.1 vs 16.6<br>0.43 (0.28-0.66)[b] |
| *BRCA*m | 22.1 vs 10.9<br>0.45 (0.32-0.64) | NR vs 10.8<br>0.40 (0.23-0.68) | 56.0 vs 13.8<br>0.33 (0.25-0.43) | NR vs 14.7<br>0.40 (0.21-0.75) | 37.2 vs 21.7<br>0.31 (0.20-0.47)[b] |
| **OS** | | | | | |
| ITT | | | | | 56.5 vs 51.6<br>0.92 (0.76-1.12) |
| HRD negative | | | | | 36.8 vs 40.4<br>1.19 (0.88-1.63) |
| HRd/Excluding *BRCA*m | | | | | NR vs 52<br>0.71 (0.45-1.13) |
| *BRCA*m | | | NR vs 75.2<br>0.55 (0.40-0.76) | | 75.2 vs 66.9<br>0.60 (0.39-0.93) |

[a] 1. Gonzalez-Martin A, et al. *N Engl J Med.* 2019;381(25):2391-2402. 2. Li N, et al. Presented at SGO 2022. Abstract 244. 3. Banerjee S, et al. *Lancet Oncol*. 2021;22(12):1721-1731. 4. Monk B, et al. JCO on line June 6, 2022. 5. Ray-Coquard I, et al. *N Engl J Med*. 2019;381(25):2416-2428. 6. Gonzalez-Martin A, et al. presented at ESMO 2022. 7. Ray-Coquard I, et al. presented at ESMO 2022. 8. DiSilvestro P, et al. presented at ESMO 2022

# Key Phase III Studies of Front-Line Intraperitoneal Therapy

| Study | N | Eligibility | Median OS | Hazard ratio | *p*-value |
|---|---|---|---|---|---|
| SWOG 8501/ GOG 104[1] | 546 | Stage III, ≤2 cm residual | IP: 49 mo<br>IV: 41 mo | 0.76 | 0.02 |
| GOG 114/ SWOG 9227[2] | 462 | Stage III, ≤1 cm residual | IP: 63.2 mo<br>IV: 52.2 mo | 0.81 | 0.05 |
| GOG 172[3] | 415 | Stage III, ≤1 cm residual | IP: 65.6 mo<br>IV: 49.7 mo | 0.75 | 0.03 |
| GOG 252[4] | 1560 | Stage II-IV, Maximal CRS | IV: 75.5 mo.<br>IPcarbo: 78.2 mo.<br>IP cis: 72.9 mo. | --<br>0.95<br>1.05 | NS |

**Retrospective analysis of GOG 114 and 172[5]**

- N = 876, median follow-up 10.7 years: Median OS for IP vs IV: **61.8 vs 51.4 mo**, HR = 0.77, *p* = 0.002

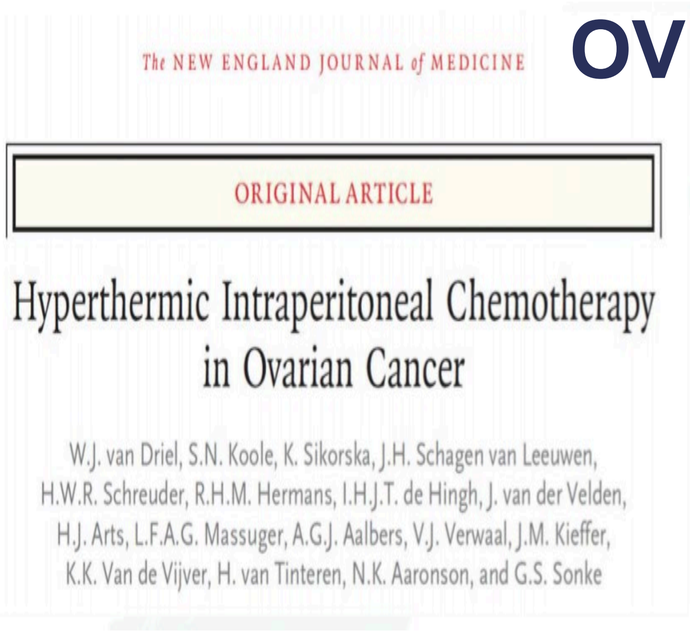
**Subgroup analysis of GOG 252[4]**

- Stage III R0/R1: Median OS for IPcarbo, IPcis vs IV: **78.2, 74.1 vs 74.6 mo**
- Stage II/III R0/R1: Median OS for IPcarbo, IPcis vs IV: **84.7, 76.3 vs 80.0 mo**
- Stage II/III R0: Median OS for IPcarbo, IPcis vs IV: **104.8, NR vs 98.8 mo**

[1] Alberts DS et al. *N Engl J Med* 1996;335:1950-5; [2] Markman M et al. *J Clin Oncol* 2001;19:1001-7; [3] Armstrong DK et al. *N Engl J Med* 2006;354:34-43; [4] Walker J et al. *J Clin Oncol* 2019;37:1380-90; [5] Tewari D et al. *J Clin Oncol* 2015;33:1460-6.

# OVHIPEC-1: Recurrence-Free and Overall Survival

NCT00426257



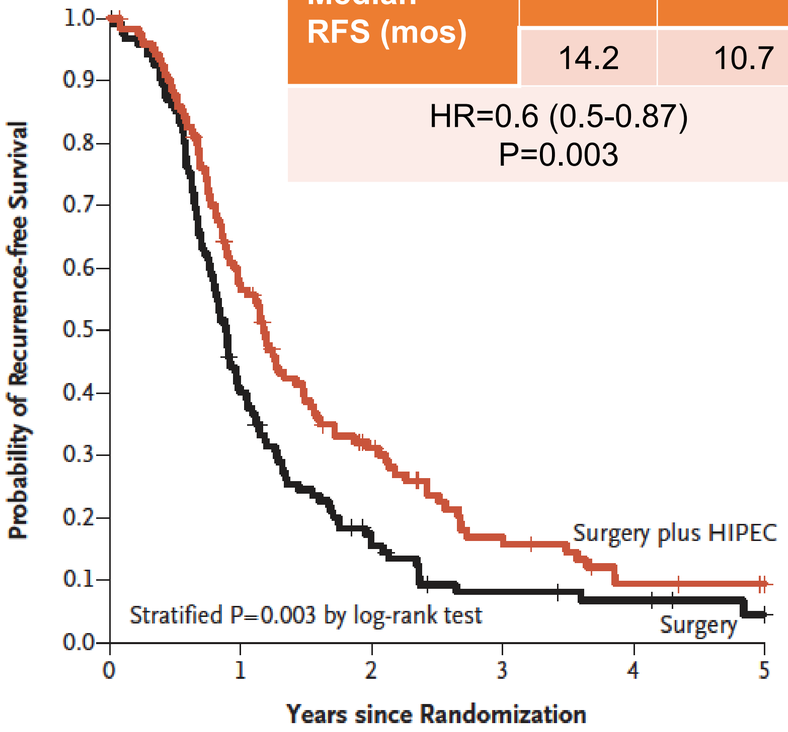

**N=245**

**Safety outcomes**
similar – Grade 3/4 toxicity 0-6% in HIPEC arm

**Elective colostomy:**
72% HIPEC vs 43% no HIPEC p=0.04

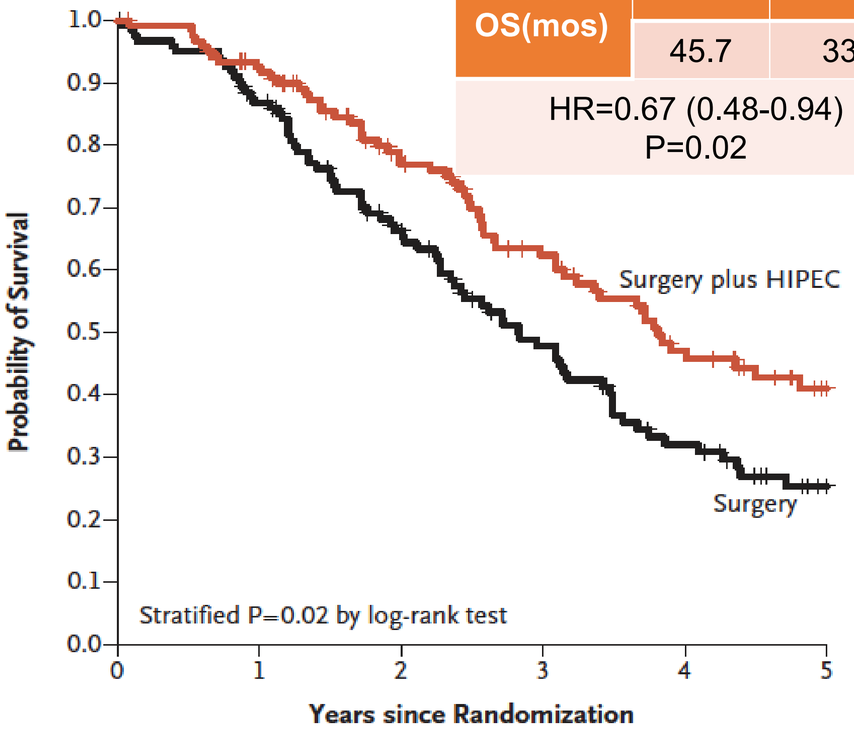
| Median RFS (mos) | HIPEC | Control |
|---|---|---|
| | 14.2 | 10.7 |

HR=0.6 (0.5-0.87)
P=0.003




| Median OS(mos) | HIPEC | Control |
|---|---|---|
| | 45.7 | 33.9 |

HR=0.67 (0.48-0.94)
P=0.02




**Dutch Gynaecological Oncology Audit Observational Study: N=668**

HIPEC: Longer LOS >7 days OR 3.9 (p<0.001) and increased complications OR 1.5 (p=0.03). No association with incidence severe complications (Clavien-Dindo ≥G3) (OR 0.7, p=0.38) and 30-day-mortality.

Van Driel *et al.* NEJM 2018; Van Stein *et al. presented at IGCS 2022*

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JAMA Surgery | Original Investigation

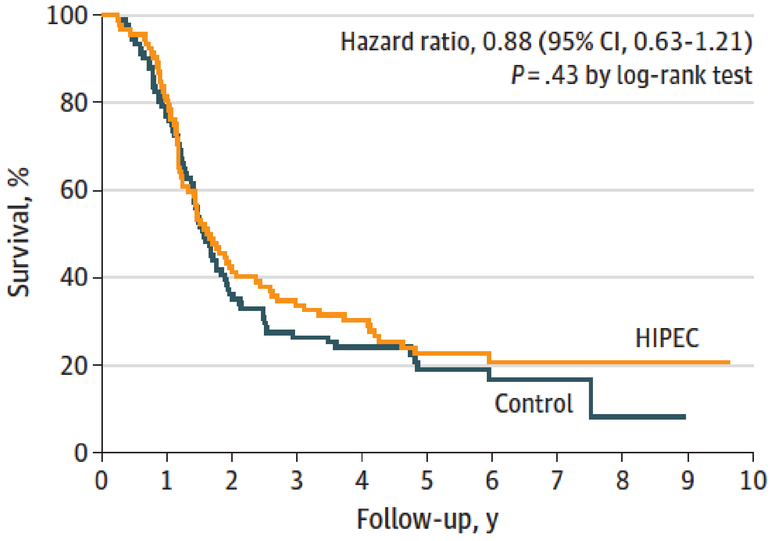
# Survival After Hyperthermic Intraperitoneal Chemotherapy and Primary or Interval Cytoreductive Surgery in Ovarian Cancer
## A Randomized Clinical Trial

JAMA Surgery

**N=184**

NCT01091636

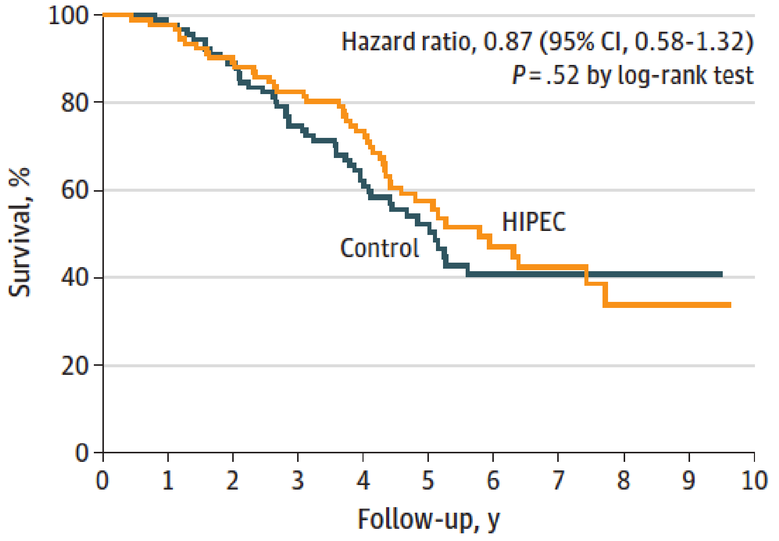
A Progression-free survival




No. at risk

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Control group | 92 | 70 | 33 | 24 | 18 | 10 | 7 | 4 | 1 | 0 | 0 |
| HIPEC group | 92 | 74 | 38 | 31 | 24 | 12 | 10 | 7 | 4 | 2 | 0 |

B Overall survival




No. at risk

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Control group | 92 | 89 | 81 | 68 | 51 | 28 | 18 | 12 | 6 | 1 | 0 |
| HIPEC group | 92 | 90 | 82 | 75 | 60 | 31 | 20 | 13 | 6 | 3 | 0 |

| Adverse Events | HIPEC N (%) | Control N (%) | *P* |
|---|---|---|---|
| Increased PT INR | 75 (81.5%) | 60 (65.2%) | 0.01 |
| Acute kidney injury | 19 (20.7%) | 6 (6.5%) | 0.005 |
| Electrolyte disturbance | 74 (80.4%) | 41 (44.6%) | 0.001 |
| Grade 3 or 4 | 86 (93.5%) | 80 (87%) | |

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JAMA Surgery | Original Investigation

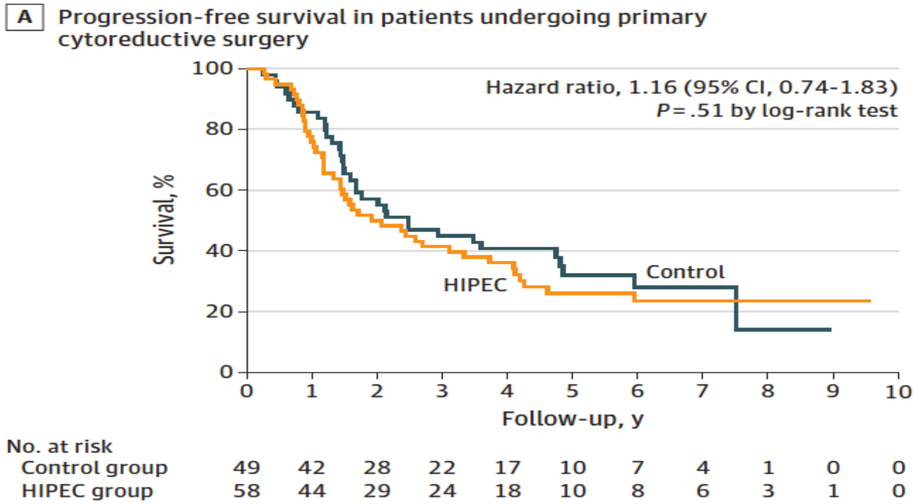
# Survival After Hyperthermic Intraperitoneal Chemotherapy and Primary or Interval Cytoreductive Surgery in Ovarian Cancer
## A Randomized Clinical Trial

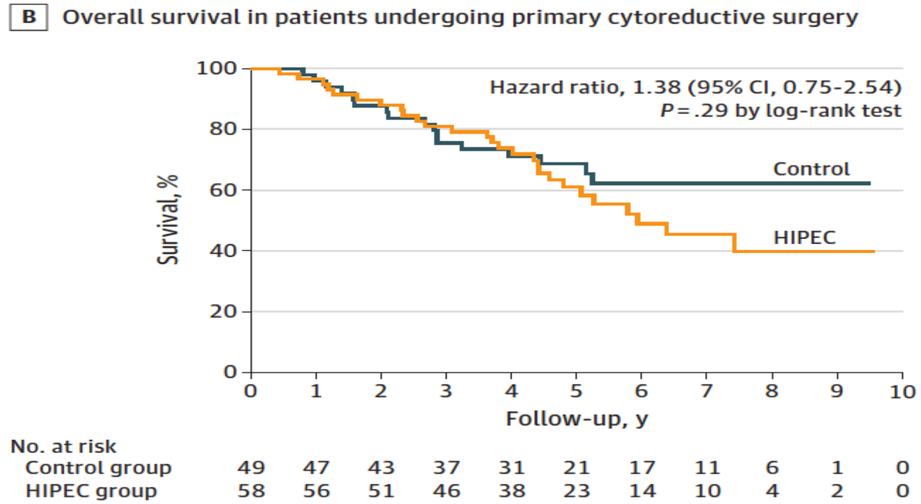
JAMA Surgery

# Subgroup Analysis: PDS and NACT/IDS

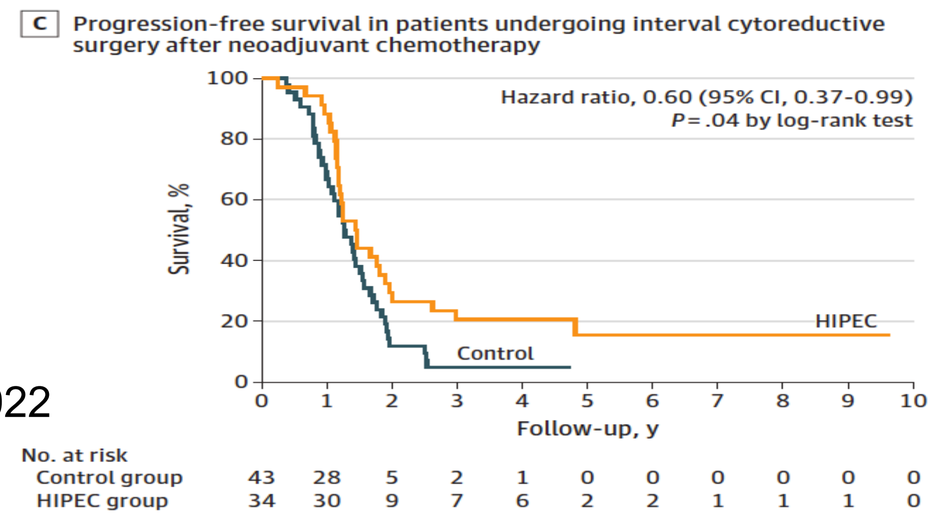
NCT01091636

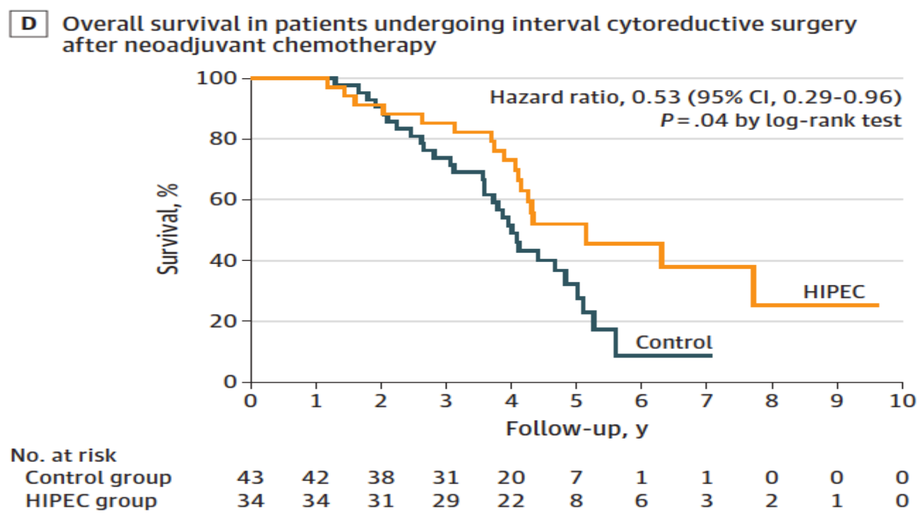
**N=107**




**N=77**

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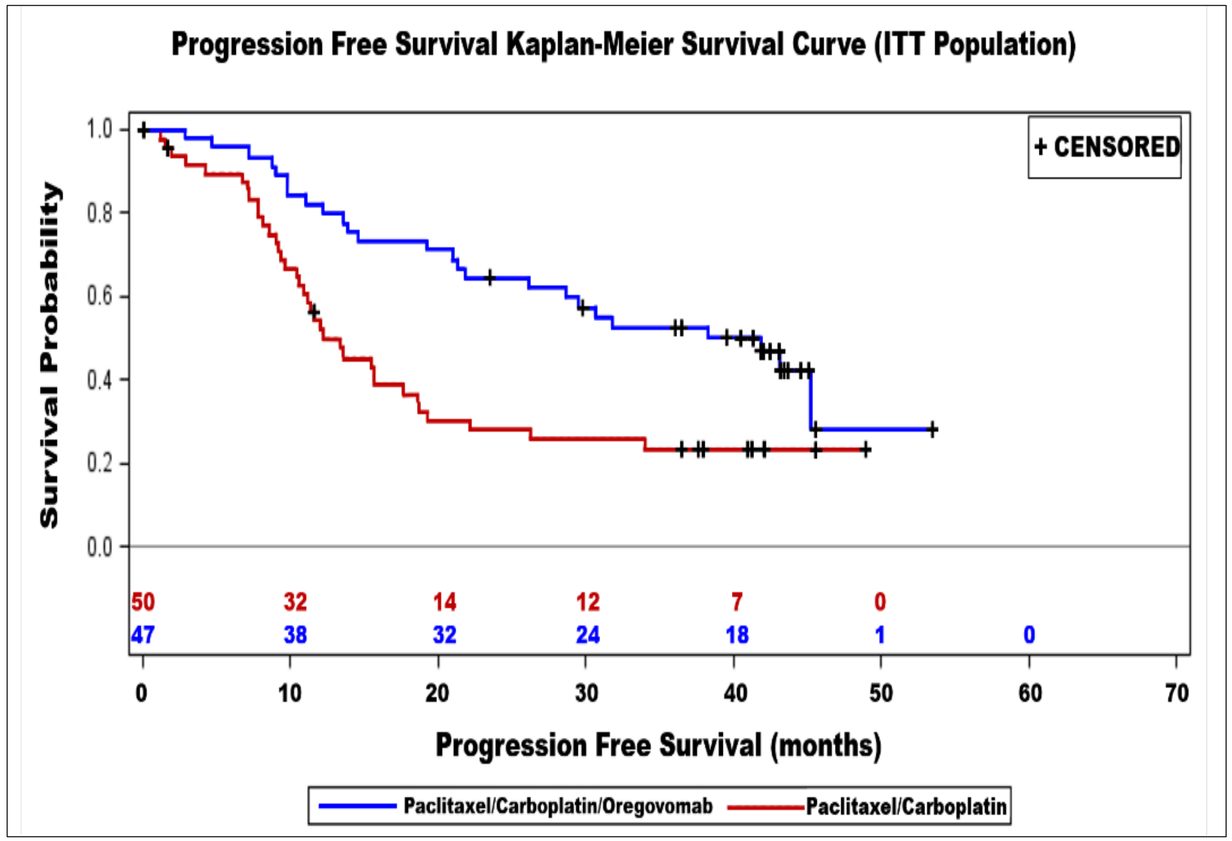
# DISCUSSION BOARD

ONE SIZE FITS ALL

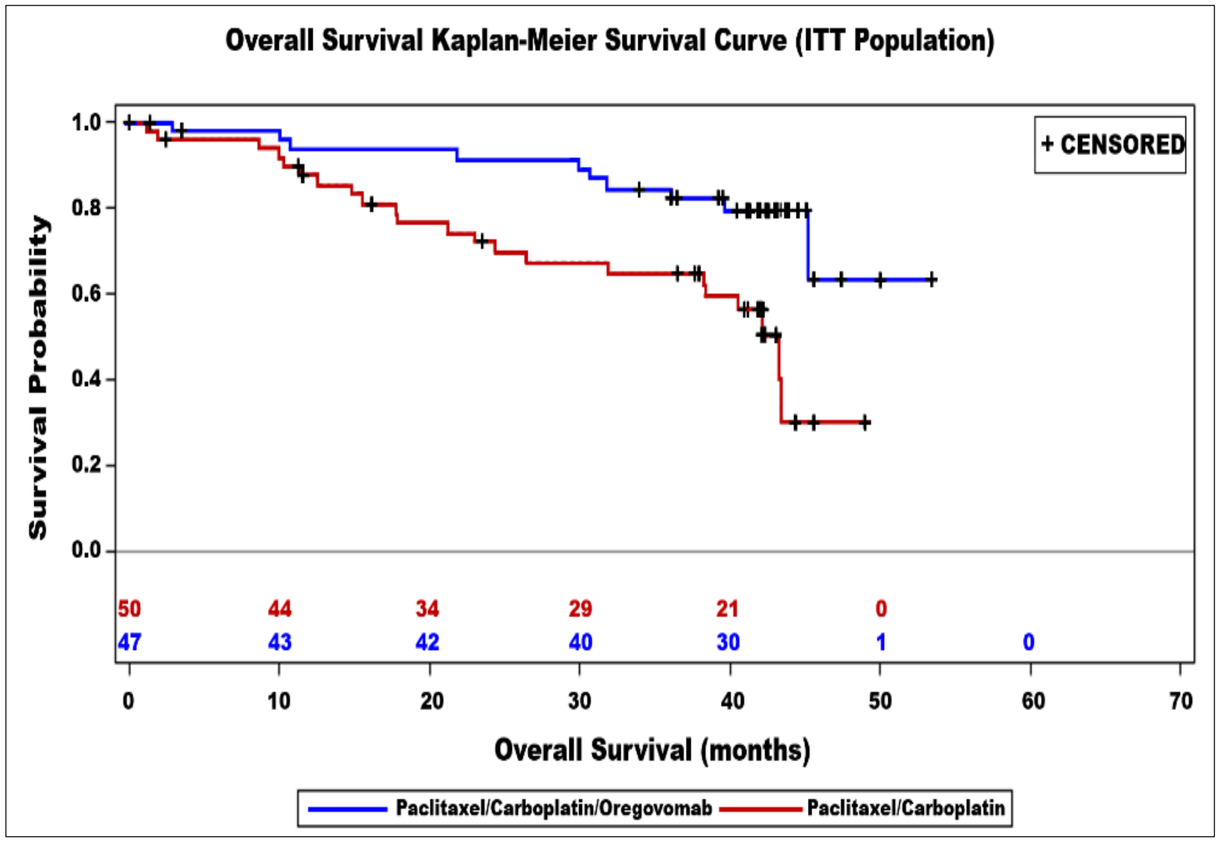
OR MAKE IT HOT

MADE TO MEASURE

# Phase 2 Randomized Clinical Trial Results (Oregovomab + Chemotherapy)




Median PFS 41.8 months (95% CI: 21.8 -NE) CPO arm and 12.2 months (95% CI: 10.4–18.6) CP arm; hazard ratio (HR) 0.46 (95% CI: 0.28–0.77), p=0.0027, log rank test




Median OS not yet estimable CPO arm, 43.2 months (95% CI: 31.8 - NE) CP arm; HR 0.35, (95% CI: 0.16–0.74) p=0.0043, log rank test

**There were no differences in the overall safety pattern between the CPO and the CP patients.**

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Brewer, M., et al (2020). Gynecol Oncol. 2020 Mar;156(3):523-529.

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# FLORA-5/QPT-ORE-005/GOG 3035

## Randomized Trial of Oregovomab and Chemotherapy in Newly Diagnosed Stage III & IV Ovarian, Primary Peritoneal, and Fallopian Tube Cancer

-Newly diagnosed stage III or IV epithelial ovarian, tubal, or peritoneal cancer

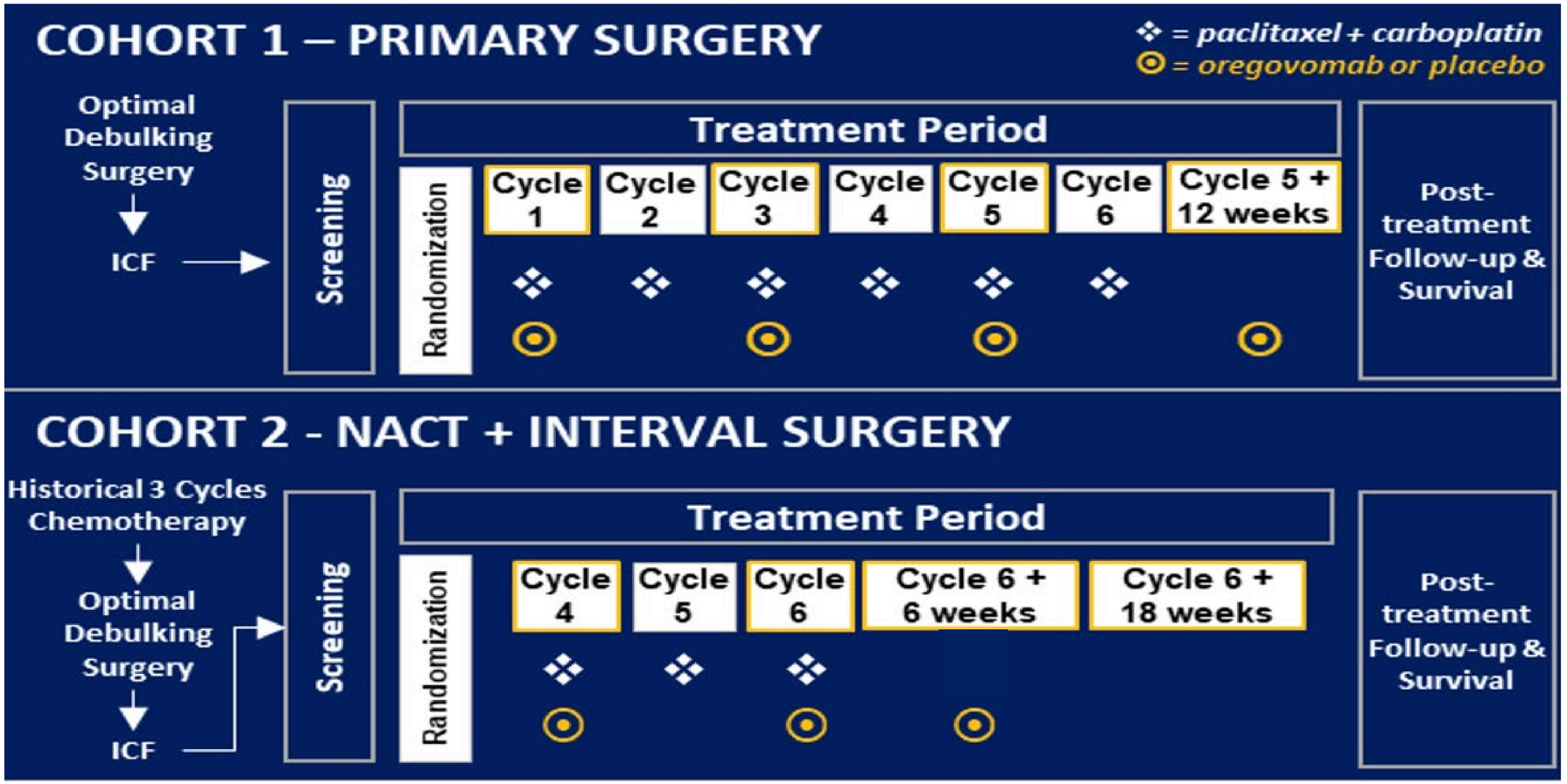
-*BRCA wild-type*

-ECOG PS 0-1

-Primary or interval cytoreductive surgery to R1 or R0

**N=602**

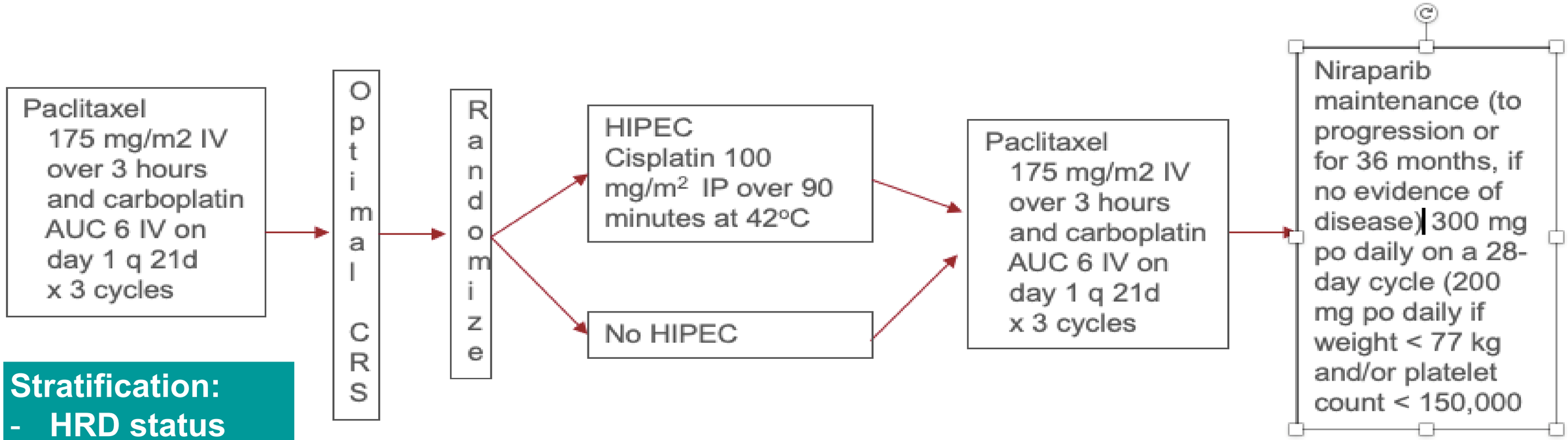
| Cohort | Total Screened | In Screening | Screening Failure | Total Randomized |
|---|---|---|---|---|
| Cohort 1 | 394 | 9 | 141 | 244 |
| Cohort 2 | 231 | 7 | 53 | 171 |




**Primary endpoint: PFS – IA; Secondary endpoints: OS, Safety, QoL**
**Exploratory: iRECIST, TFST, TSST, PFS2, Biomarkers**

# HOTT/GOG 3068: HIPEC in Ovarian Treatment Trial

## Randomized Trial of Hyperthermic Intraperitoneal Chemotherapy (HIPEC) with Cisplatin vs. no HIPEC at Time of Optimal Interval Cytoreductive Surgery followed by Niraparib Maintenance in Newly Diagnosed Stage III & IV Ovarian, Primary Peritoneal, and Fallopian Tube Cancer




**Stratification:**
- **HRD status**
- **R0 vs R1**
- **Stage (III vs IV)**

**Primary endpoint: PFS**
**Secondary endpoints: OS, Toxicity, Prognostic effects of HRD, R0/1, Stage III/IV**

**PI: Zivanovic O, Randall L**

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# THANK YOU

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