



18^{as} Jornadas HITOS
ONCOLÓGICOS: LO
MEJOR DE **2023**

Madrid, 22 y 23 de noviembre de 2023

Cambio del paradigma en el cáncer de ovario: IPARPs

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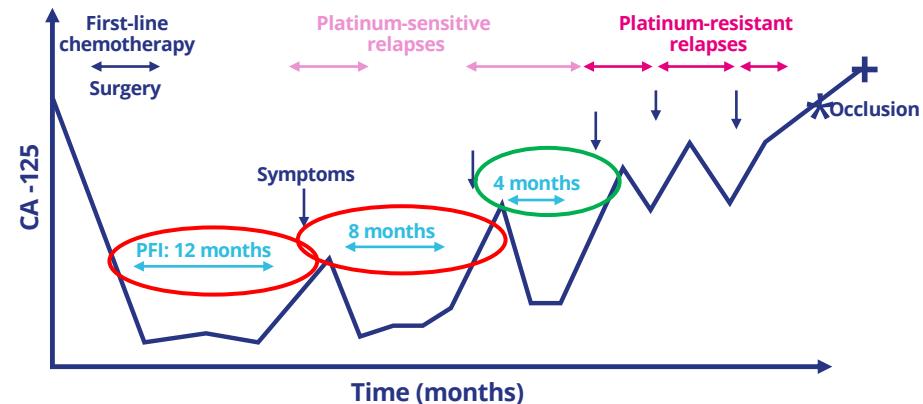


DISCLOSURE SLIDE

- Employment: Hosp. Univ. 12 de Octubre
- Consultant or Advisory Role: Lilly, GSK, Clovis, Astra-Zeneca, Roche, Novartis, Pfizer.
- Research Funding: Tesaro-GSK
- Speaking: Lilly, Roche, Astra-Zeneca, Novartis, Pfizer, GSK, Clovis

Advanced ovarian cancer: a “chronic” disease with multiple relapses

- Ovarian cancer (OC) is the most lethal gynecologic cancer
- 300.000 women were diagnosed worldwide with OC in 2020
- ≥60% of newly diagnosed women will have advanced disease
- ~70% of women relapse within 3 years of first-line treatment
- 5-year survival for newly diagnosed advanced OC is about 30-50%
- There is a significant need for better first-line treatment to improve outcomes for women with OC



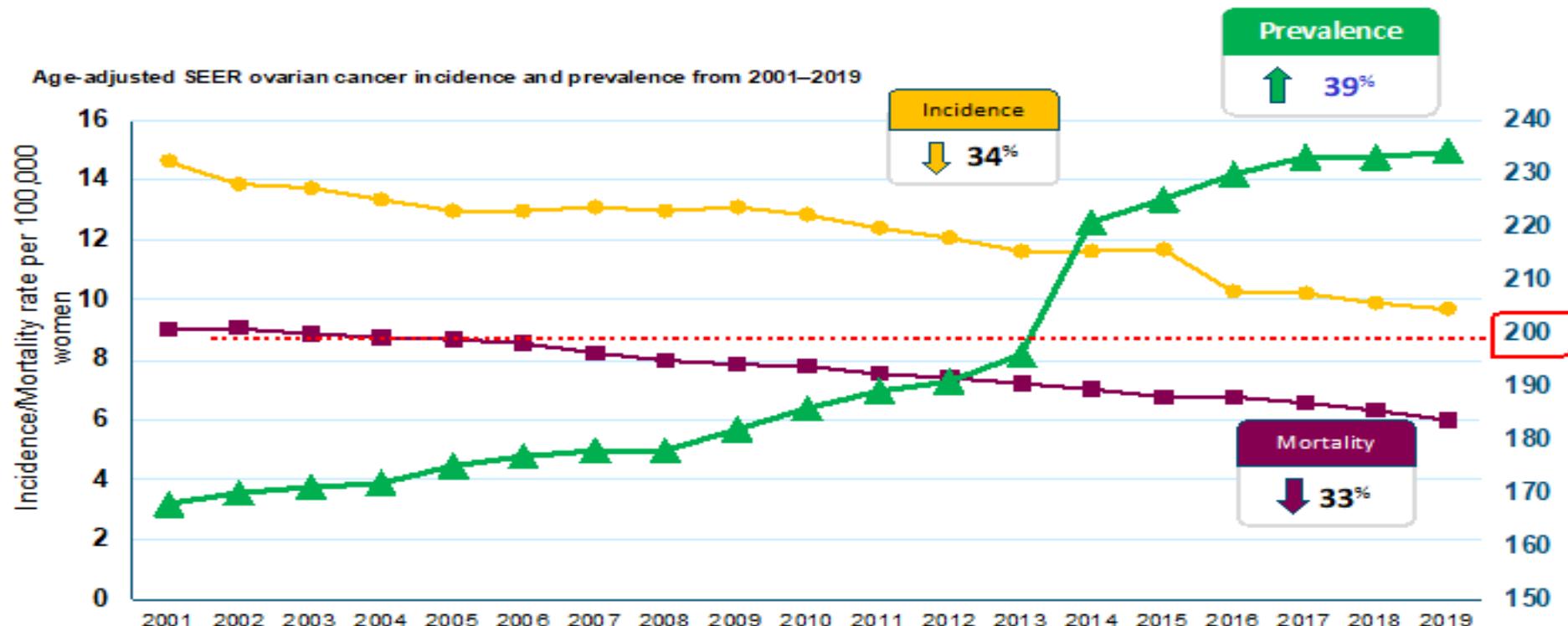
Recent ovarian cancer epidemiology

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Ovarian Cancer: Clinical Impact

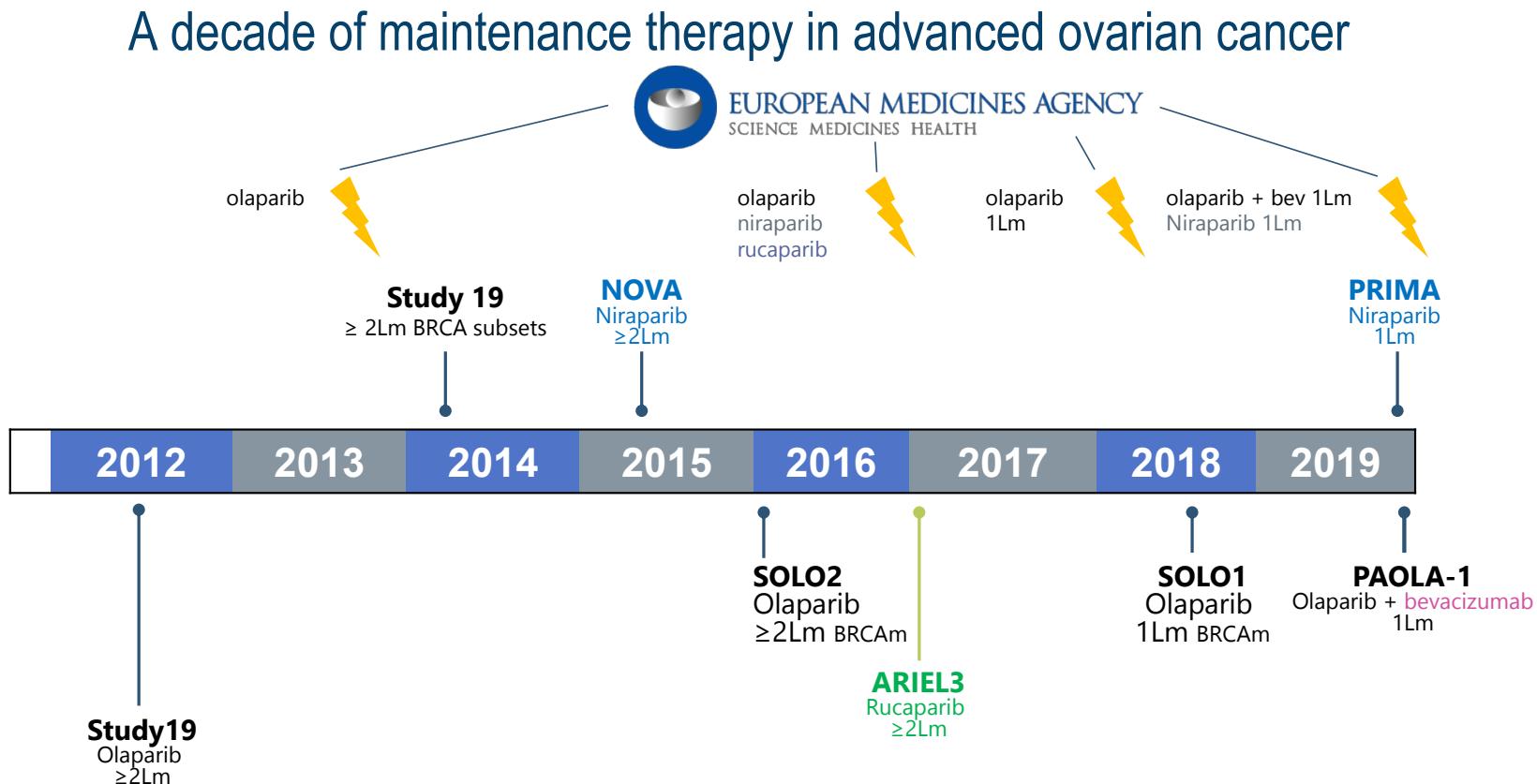


https://seer.cancer.gov/statisticsnetwork/explorer/application.html?site=61&data_type=9&graph_type=2&compareBy=rate_type&chk_rate_type_1=1&chk_rate_type_2=2&chk_rate_type_3=3&hdn_sex=3&race=1&age_range=1&hdn_stage=101&advopt_precision=1&advopt_show_ci=on&hdn_view=0&advopt_display=2



BRCA mutations open the door to biomarker directed therapy of ovarian cancer

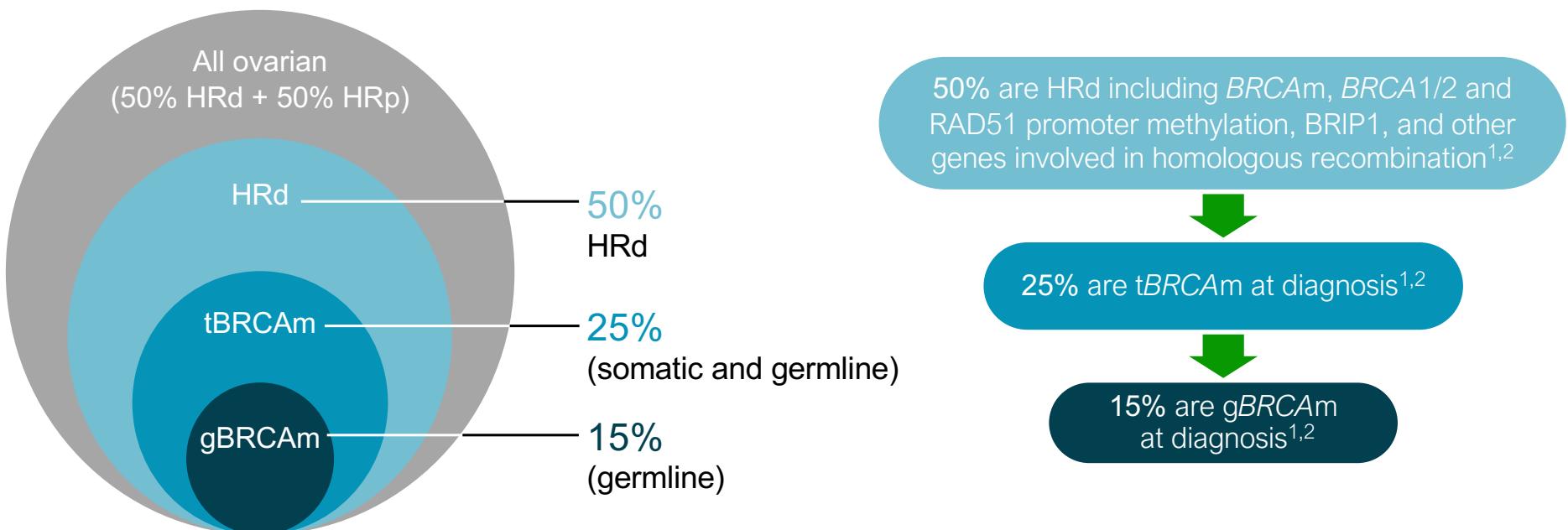
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1. Ledermann J, et al. N Engl J Med 2012;366:1382–92; 2. Ledermann et al Lancet Oncol 2014 15: 852-61. 3. Mirza MR, et al. N Engl J Med 2016;375:2154–64;; 4. Pujade- Lauraine E, et al. Lancet Oncol 2017;18:1274–84; 5. Coleman R, et al. Lancet 2017;390:1949–61; 6. Moore K, et al. N Engl J Med 2018;379:2495–505; 7. González Martín A, et al. N Engl J Med 2019;381:2391–402; 8. Ray-Coquard I, et al. N Engl J Med 2019;381:2416–28

Biomarkers play an important role in diagnosing and defining patient populations in ovarian cancer

Half of high-grade serous OC exhibits a high degree of genomic instability due to deficiencies in homologous recombination



BRCA, breast cancer gene; *BRIP*1, *BRCA*1-interacting protein; g*BRCA*m, germline *BRCA* mutant; HRd, homologous recombination deficient; HRp, homologous recombination proficient; OC, ovarian cancer; t*BRCA*m, tumour *BRCA* mutant.

1. Abkevich V, et al. Br J Cancer 2012;107:1776–82; 2. The Cancer Genome Atlas Research Network. Nature 2011;474:609–15.



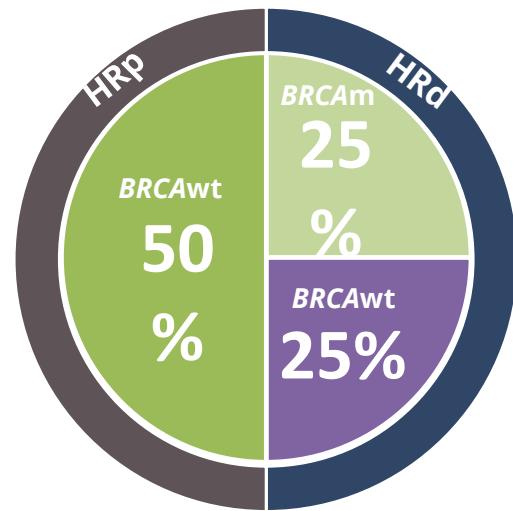
Positioning PARP inhibitors in the treatment of ovarian cancer

	SOLO-1 (Olaparib)	PRIMA (Niraparib)	PAOLA-1 (Olaparib + Bevacizumab)	PRIME (Niraparib)	ATHENA-MONO (Rucaparib)
Population HRD test	N=391 BRCA Analysis test (Myriad) / BGI (China)	N=733 myChoice®: BRCAm or HRD score ≥42	N=806 myChoice®: BRCAm or HRD score ≥42	N=384 BGI Assay (BGI genomics)	N=538 FoundationOne CDx: BRCAm or LOH≥16%
Prior surgical status	Stage III PDS or IDS Stage IV no limitation	Stage III PDS R>0 Stage III IDS Stage IV	No limitation	No limitation	PDS or IDS
Response criteria	CR/PR after platinum	CR/PR after platinum PR >2 cm excluded Normal or >90% ↓ CA-125	CR/PR after platinum	CR/PR after platinum (irrespective of RD)	CR/PR after platinum
Control arm	Placebo	Placebo	Pbo + Bevacizumab	Placebo	Placebo
Duration PARPi	2 years	3 years	2 years	3 years	2 years



Rationale for PARP inhibitors in ovarian cancer

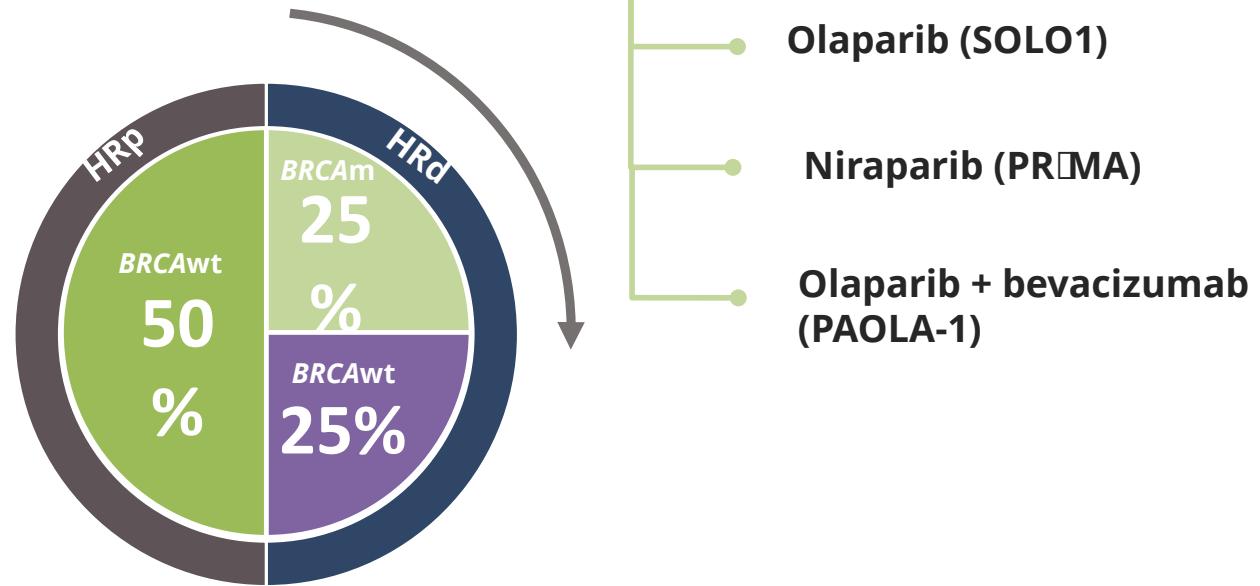
Maintenance options





Rationale for PARP inhibitors in ovarian cancer

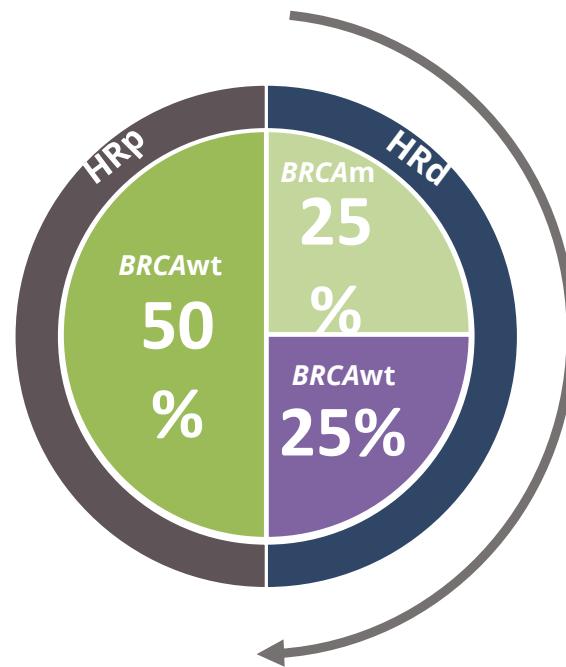
Maintenance options





Rationale for PARP inhibitors in ovarian cancer

Maintenance options



BRCAm/HRD

Olaparib (SOLO1)

Niraparib (PRIMA)

Olaparib + bevacizumab
(PAOLA-1)

BRCAwt/HRD

Niraparib (PRIMA)

Olaparib + bevacizumab
(PAOLA-1)

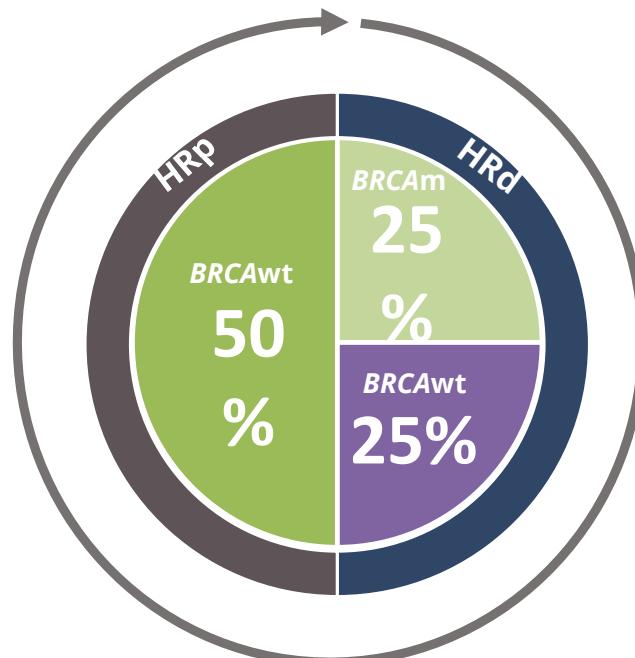


Rationale for PARP inhibitors in ovarian cancer

HRp

- Bevacizumab (GOG-0218/ICON7)
- Niraparib (PRIMA)

Maintenance options



BRCAm/HRd

- Olaparib (SOLO1)
- Niraparib (PRIMA)
- Olaparib + bevacizumab (PAOLA-1)

BRCAwt/HRD

- Niraparib (PRIMA)
- Olaparib + bevacizumab (PAOLA-1)



Rationale for PARP inhibitors in ovarian cancer

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Magnitude of benefit with PARPi is related to biomarker
Even patients with HRp (HRD-) benefit from PARPi

	SOLO-1¹	PRIMA²	PAOLA-1³	ATHENA-MONO⁴	PRIME⁵
PARPi	Olaparib	Niraparib	Olaparib + Bev	Rucaparib	Niraparib
Control	Placebo	Placebo	Bevacizumab	Placebo	Placebo
Population	BRCAmut	All comers	All comers	All comers	All comers (Chinese)
HRD test	NA	MyChoice	MyChoice	Foundation-One	BGI
+++	BRCAmut	0.33 (0.25–0.43)	0.40* (0.27–0.62)	0.31* (0.20–0.47)	0.31* (0.20–0.47)
++	BRCAwt/HRD+	-	0.50* (0.31-0.83)	0.43* (0.28-0.66)	0.58* (0.33-1.01)
+	BRCAwt/HRD-	-	0.68* (0.49-0.94)	0.92* (0.72-1.17)	0.65* (0.45-0.95)

*exploratory

The aim of the table is not the cross-trial comparison



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- TIPO MOLECULARES Y POBLACIONES DE RIESGO.
- INMUNOTERAPIA + iPARPs: 1 LINEA Y RECAIDA.
- LARGOS RESPONDEDORES.



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- TIPO MOLECULARES Y POBLACIONES DE RIESGO.
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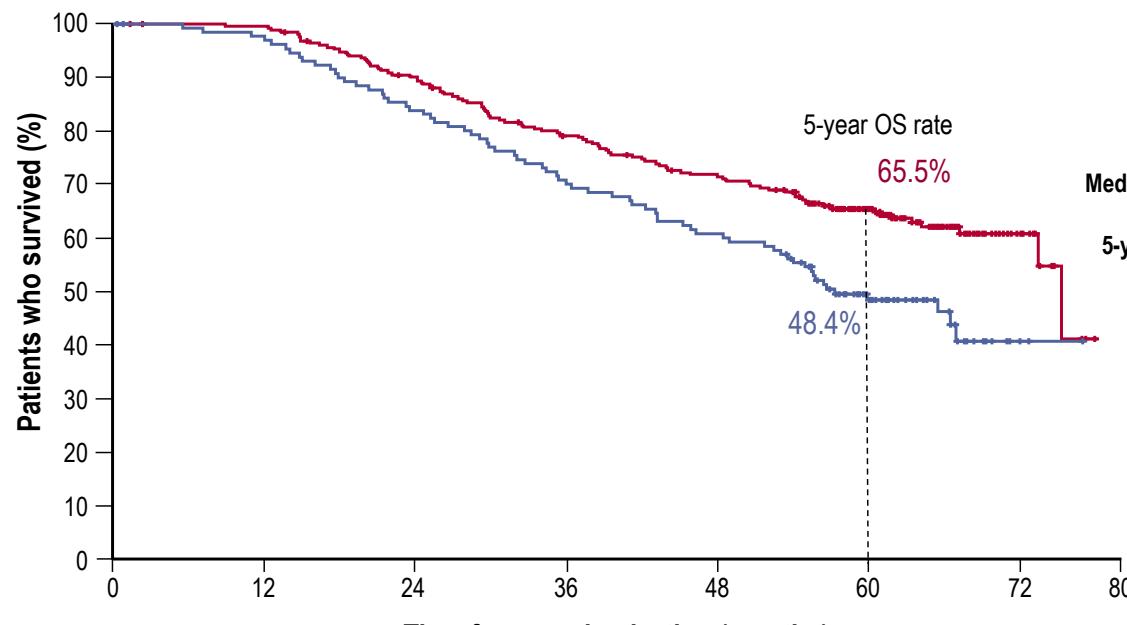
Rationale for PARP inhibitors in ovarian cancer

BRCAm/HRD

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PAOLA-1/ENGOT-ov25

OS was prolonged in the HRD-positive subgroup



Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
93 (36.5)	69 (52.3)
75.2 (unstable)*	57.3
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)	

*Median unstable; <50% data maturity.

PARIS ESMO congress

Isabelle Ray-Coquard

HRD positive defined as a tBRCAm and/or genomic instability score of ≥42 on the Myriad myChoice HRD Plus assay.

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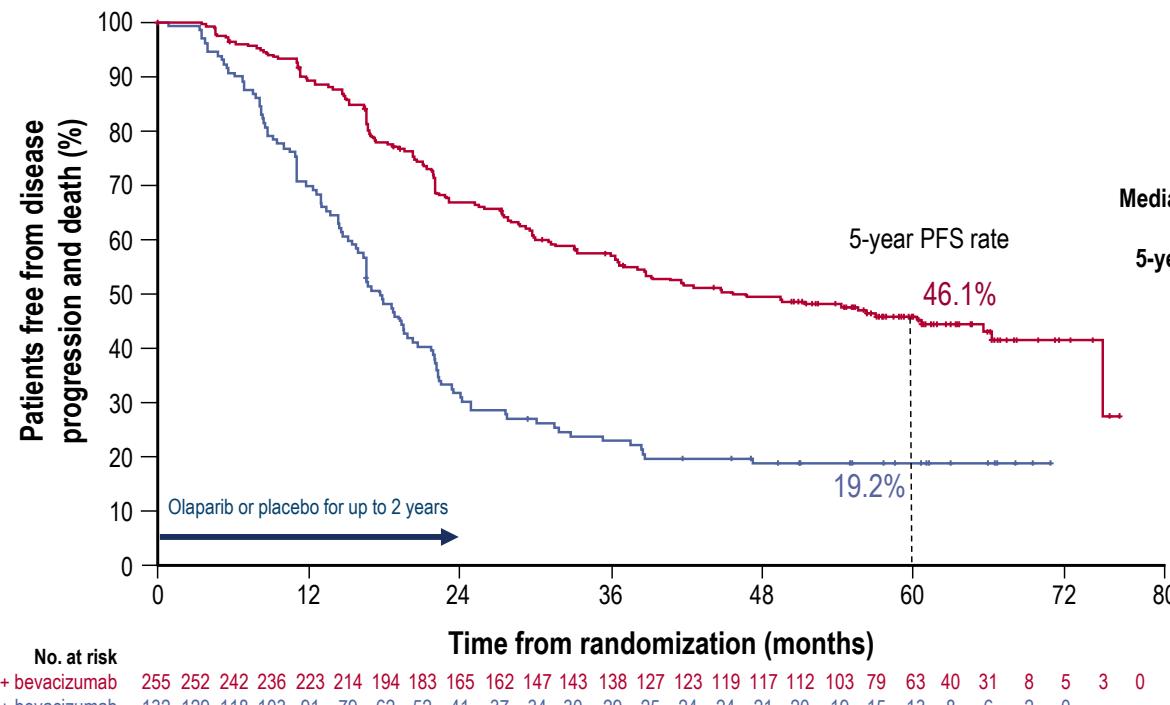
Rationale for PARP inhibitors in ovarian cancer

BRCAm/HRD

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PAOLA-1/ENGOT-ov25

Updated PFS: HRD-positive population*



Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
136 (53.3)	104 (78.8)
46.8	17.6
46.1	19.2
HR 0.41 (95% CI 0.32–0.54)	
59% reduction in risk of disease progression or death for olaparib + bevacizumab vs bevacizumab alone	



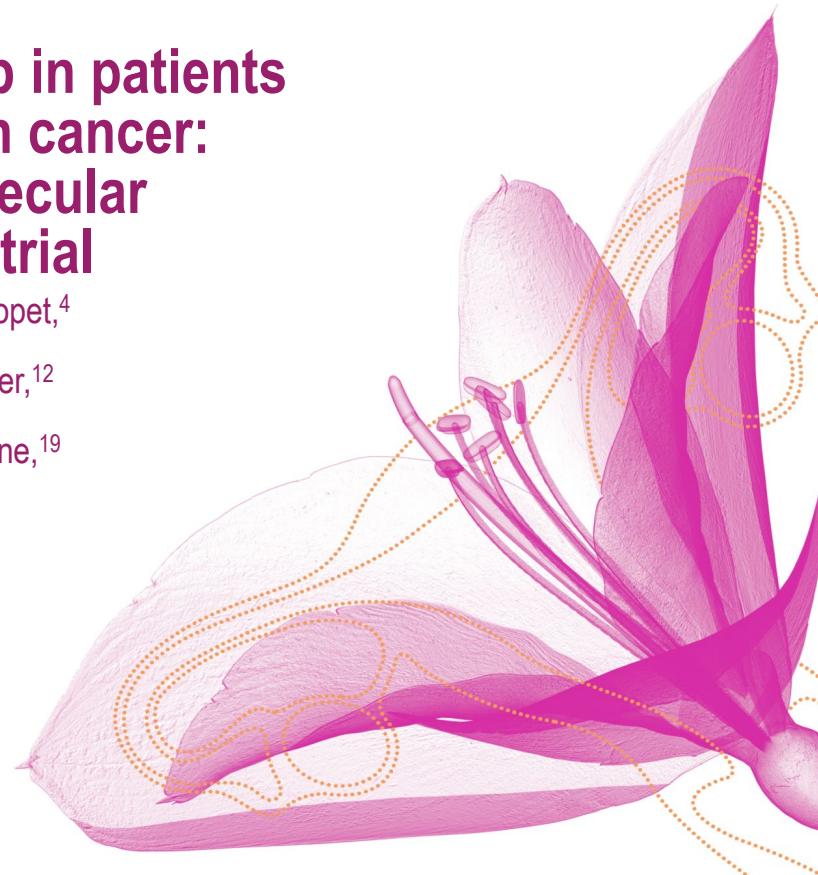
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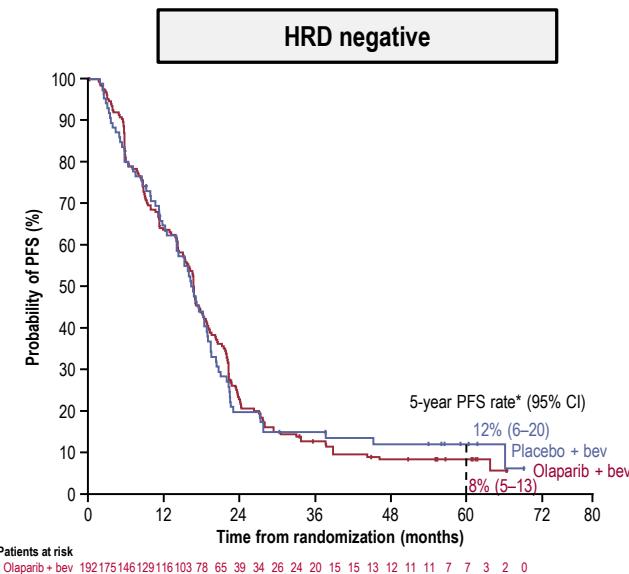
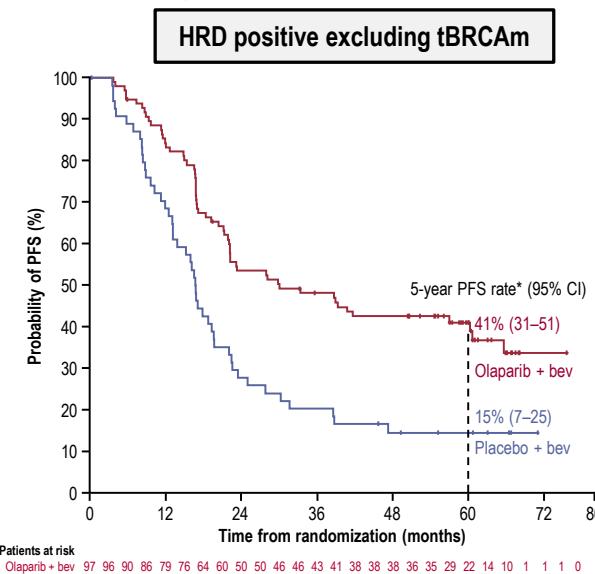
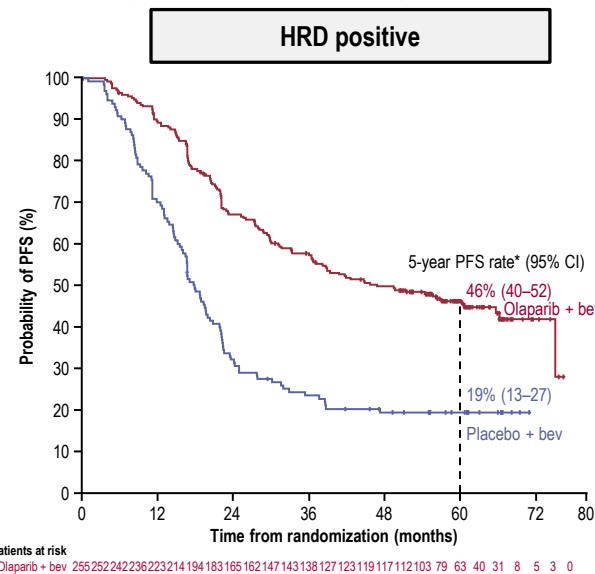
Maintenance olaparib plus bevacizumab in patients with newly diagnosed advanced ovarian cancer: 5-year progression-free survival by molecular subgroup in the PAOLA-1/ENGOT-ov25 trial

Antonio González-Martín,¹ Jacques Medioni,² Philipp Harter,³ Claire Cropet,⁴ Saverio Cinieri,⁵ Ursula Denison,⁶ Hiroyuki Fujiwara,⁷ Ignace Vergote,⁸ Alessandra Bologna,⁹ Sakari Hietanen,¹⁰ Manuel Rodrigues,¹¹ Lars Hanker,¹² Claudio Zamagni,¹³ Susana Hernando-Polo,¹⁴ Diana Bello Roufai,¹⁵ Dirk Bauerschlag,¹⁶ Benoît You,¹⁷ Peter Hillemanns,¹⁸ Eric Pujade-Lauraine,¹⁹ Isabelle Ray-Coquard²⁰

¹Clinica Universidad de Navarra, Navarra, and GEICO, Spain; ²Hôpital Européen Georges Pompidou, Paris, and GINECO, France; ³Kliniken Essen-Mitte, Essen, and AGO, Germany; ⁴Centre Léon Berard, Lyon, France; ⁵UOC Oncología Médica – Ospedale Senatore Antonio Perrino, Brindisi, and MITO, Italy; ⁶Institute for Gynaecological Oncology und Senology – Karl Landsteiner, Klinik Hietzing, Vienna, and AGO AU, Austria; ⁷Jichi Medical University, Tochigi, and GOTIC, Japan; ⁸University Hospital Leuven, Leuven Cancer Institute, Leuven, and BGOG, Belgium; ⁹Azienda USL – IRCCS di Reggio Emilia, and MANGO, Italy; ¹⁰Turku University Hospital, and NSGO, Finland; ¹¹Institut Curie – Hôpital Claudius Régaud, Paris, and GINECO, France; ¹²Universitätsklinikum Schleswig-Holstein, Universitätsfrauenklinik, Campus Lübeck, and AGO, Germany; ¹³IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, and MITO, Italy; ¹⁴Fundación Hospital de Alcorcón, Madrid and GEICO, Spain; ¹⁵Institut Curie – Saint-Cloud, Paris, and GINECO, France; ¹⁶University Medical Center Schleswig-Holstein, UKSH, Campus Kiel, and AGO, Germany; ¹⁷Centre Hospitalier Lyon Sud, Pierre-Bénite, and GINECO, France; ¹⁸Dedizinische Hochschule Hannover, Hannover, and AGO, Germany; ¹⁹ARCAGY Research, Paris, and GINECO, France; ²⁰Centre Léon Berard, Lyon, and GINECO, France



5-year PFS by molecular subgroup



Olaparib + bev (N=255)	Placebo + bev (N=132)
---------------------------	--------------------------

Events, n (%)	136 (53)	104 (79)
Median PFS, months	46.8	17.6
HR (95% CI)	0.41 (0.32-0.54)	

Olaparib + bev (N=97)	Placebo + bev (N=55)
--------------------------	-------------------------

Events, n (%)	58 (60)	46 (84)
Median PFS, months	30.0	16.6
HR (95% CI)	0.47 (0.32-0.70)	

Olaparib + bev (N=192)	Placebo + bev (N=85)
---------------------------	-------------------------

Events, n (%)	167 (87)	74 (87)
Median PFS, months	16.6	16.2
HR (95% CI)	1.01 (0.77-1.33)	

- Most patients without relapse at 5 years are potentially cured
- To help inform the potential for cure, we evaluated 5-year PFS according to molecular subgroups in a *post hoc*, updated, descriptive analysis conducted at the final OS DCO

*Calculated by KM estimates.

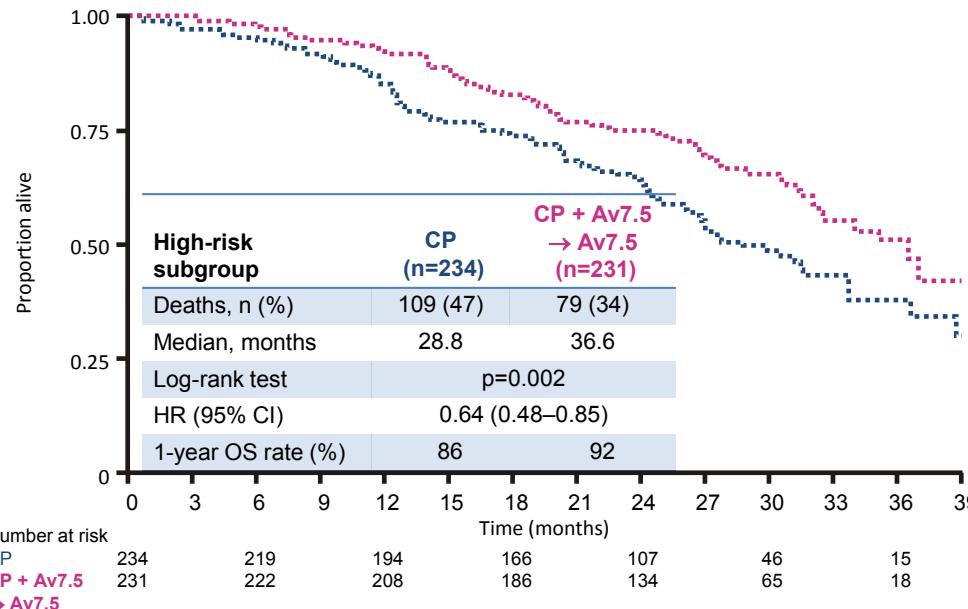
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Antonio González-Martín

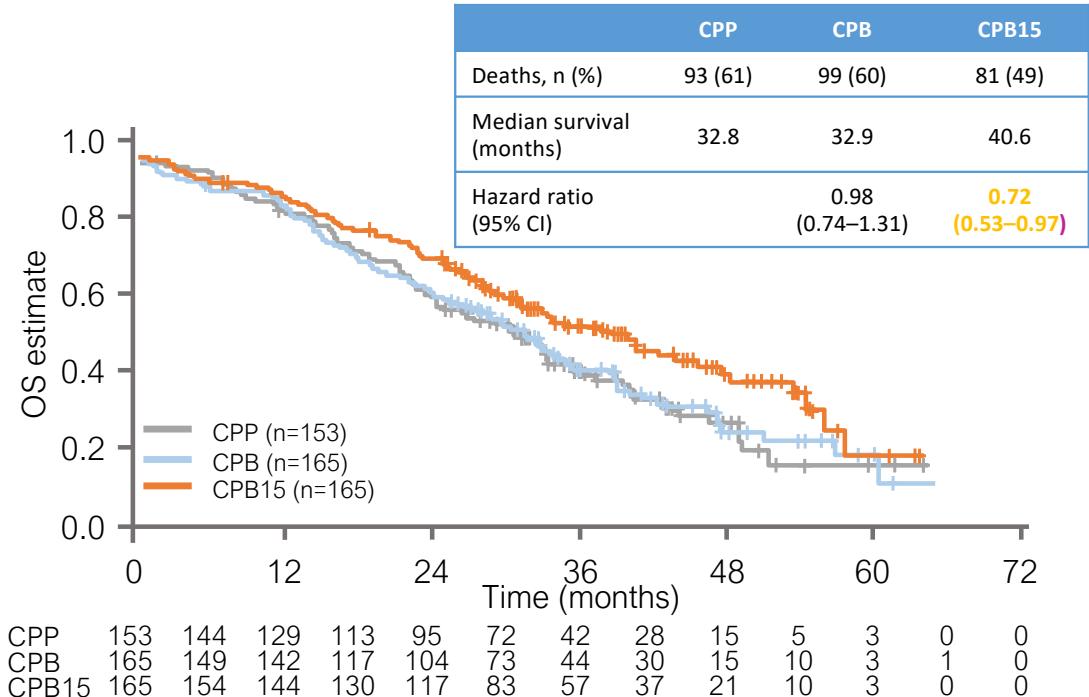


Rationale for PARP inhibitors in ovarian cancer

ICON-7: OS in patients at high risk for progression¹



GOG-0218: OS in patients at high risk for progression²



Bevacizumab monotherapy is an important 1L standard of care which is typically reserved for certain higher-risk patients

Extending bevacizumab duration from 15 to 30 months provided no added benefit (BOOST trial)⁴

1. Perren TJ, et al. N Engl J Med 2011;365:2484–96; 2. Randall L, et al. presented at SGO 2013, 7–12 Mar, Los Angeles, CA.



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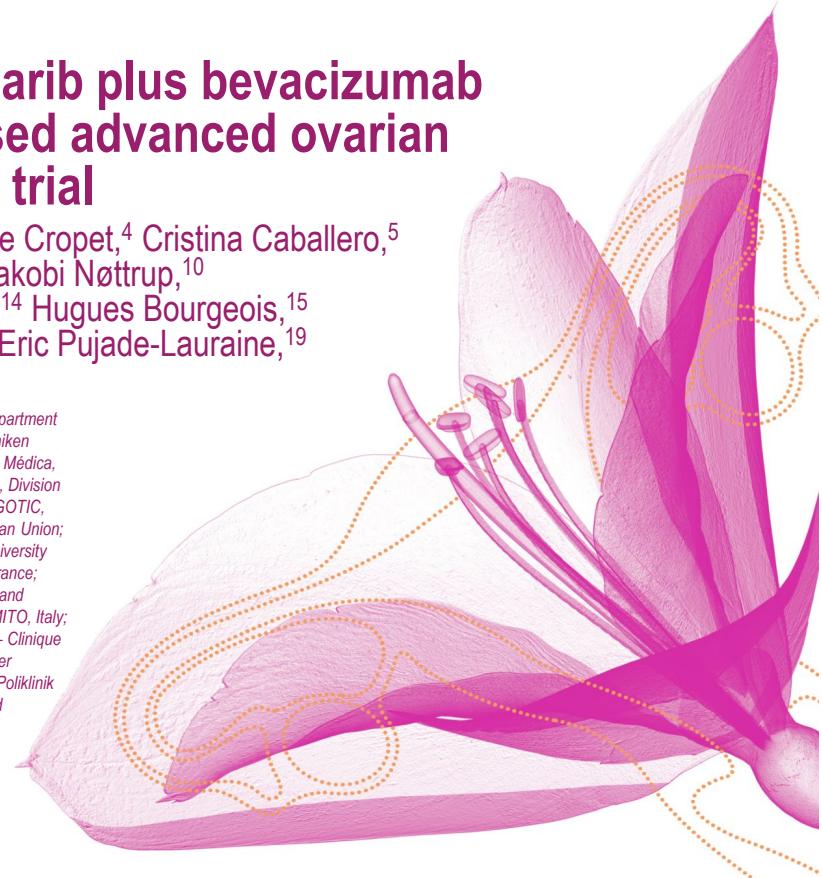
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5-year overall survival with maintenance olaparib plus bevacizumab by clinical risk in patients with newly diagnosed advanced ovarian cancer in the Phase III PAOLA-1/ENGOT-ov25 trial

Domenica Lorusso,¹ Marie-Ange Mouret-Reynier,² Philipp Harter,³ Claire Cropet,⁴ Cristina Caballero,⁵ Edgar Petru,⁶ Toyomi Satoh,⁷ Ignace Vergote,⁸ Gabriella Parma,⁹ Trine Jakobi Nøttrup,¹⁰ Coriolan Lebreton,¹¹ Peter A. Fasching,¹² Carmela Pisano,¹³ Luis Manso,¹⁴ Hugues Bourgeois,¹⁵ Ingo Runnebaum,¹⁶ Anne-Claire Hardy-Bessard,¹⁷ Andreas Schnelzer,¹⁸ Eric Pujade-Lauraine,¹⁹ Isabelle Ray-Coquard²⁰

¹Istituto Tumori Milano + Fondazione Policlinico Universitario A Gemelli IRCCS, Rome, Catholic University of Sacred Heart, and MITO, Italy; ²Department of Medical Oncology, Centre Jean Perrin, Clermont Ferrand, and GINECO, France; ³Department of Gynaecology & Gynaecologic Oncology, Kliniken Essen-Mitte, Essen, and AGO, Germany; ⁴Department of Biostatistics, Centre Léon Berard, Lyon, and GINECO, France; ⁵Servicio de Oncología Médica, Hospital General Universitario de Valencia, Valencia, and GEICO, Spain; ⁶Department of Obstetrics and Gynecology, Medical University of Graz, Division of Gynecology, Graz, and AGO, Austria; ⁷Department of Obstetrics and Gynecology, Faculty of Medicine, University of Tsukuba, Tsukuba, and GOTIC, Japan; ⁸Department of Obstetrics and Gynaecology, University Hospital Leuven, Leuven Cancer Institute, Leuven, and BGOG, Belgium, European Union; ⁹Gynecologic Oncology Program, European Institute of Oncology IRCCS, Milan, and MANGO, Italy; ¹⁰Department of Oncology, Copenhagen University Hospital - Rigshospitalet, Copenhagen, and NSGO, Denmark; ¹¹Department of Medical Oncology, Institut Bergonié, Bordeaux, and GINECO, France; ¹²Gynecology and Obstetrics Translational Medicine, Universitätsfrauenklinik Erlangen, Erlangen, and AGO, Germany; ¹³Department of Urology and Gynecology, Istituto Nazionale Tumori, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS)-Fondazione G. Pascale Napoli, Naples, and MITO, Italy; ¹⁴Department of Medical Oncology; Hospital 12 de Octubre, Madrid, and GEICO, Spain; ¹⁵Medical Oncology Department, Centre Jean Bernard – Clinique Victor Hugo, Le Mans, and GINECO, France; ¹⁶Department of Gynecology and Reproductive Medicine, Jena University Hospital, Friedrich Schiller University, and AGO, Germany; ¹⁷Oncologie Médicale, Centre CARIO - HPCA, Plérin Sur Mer, Plérin, and GINECO, France; ¹⁸Frauenklinik und Poliklinik Klinikum rechts der Isar, Technische Universität München, and AGO, Germany; ¹⁹Medical Oncology Department, ARCAGY Research, Paris, and GINECO, France; ²⁰Department of Medical Oncology, Centre Léon Berard, Lyon, and GINECO, France

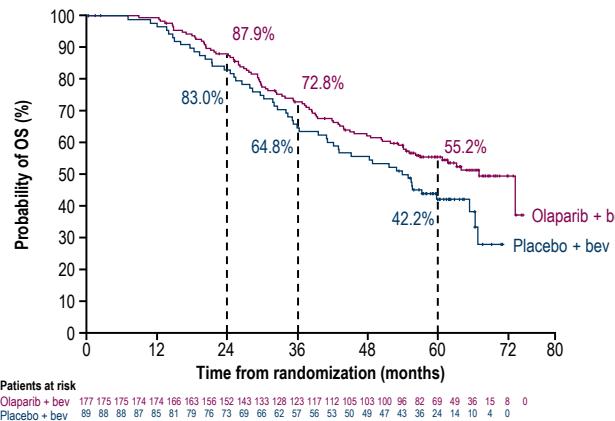
ClinicalTrials.gov identifier: NCT02477644 | This study was sponsored by ARCAGY Research



5-year OS by clinical risk in HRD-positive patients

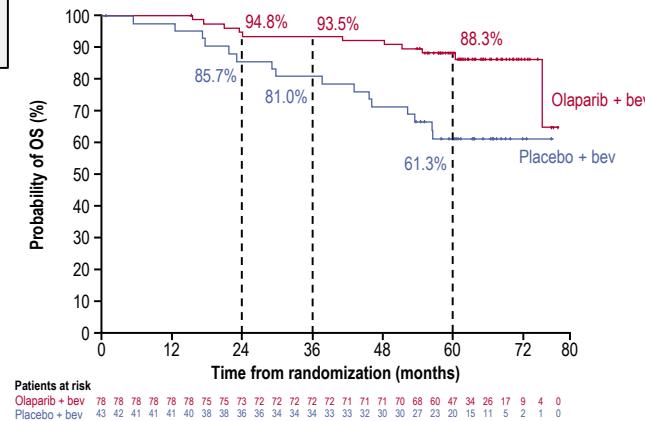
Higher risk

FIGO stage III disease who had undergone upfront surgery and had residual disease or who had received neoadjuvant chemotherapy, or FIGO stage IV patients



Lower risk

FIGO stage III PDS & RO



Events, n (%)

	Olaparib + bevacizumab (n=177)	Placebo + bevacizumab (n=89)
Events, n (%)	82 (46.3)	53 (59.6)
Median OS, months	67.0*	54.0
5-year OS rate, %	55.2	42.2
	HR 0.70 (95% CI 0.50–1.00)	

Patients receiving a PARP inhibitor during any subsequent treatment, %

	Olaparib + bevacizumab (n=177)	Placebo + bevacizumab (n=89)
Patients receiving a PARP inhibitor during any subsequent treatment, %	18.6	56.2

Events, n (%)

	Olaparib + bevacizumab (n=78)	Placebo + bevacizumab (n=43)
Events, n (%)	11 (14.1)	16 (37.2)
Median OS, months	NE	NE
5-year OS rate, %	88.3	61.3
	HR 0.31 (95% CI 0.14–0.66)	

Patients receiving a PARP inhibitor during any subsequent treatment, %

	Olaparib + bevacizumab (n=78)	Placebo + bevacizumab (n=43)
Patients receiving a PARP inhibitor during any subsequent treatment, %	14.1	39.5

HRD positive defined as a tBRCAm and/or genomic instability score of ≥ 42 on the Myriad myChoice HRD Plus assay.

*Median unstable because of a lack of events.

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Domenica Lorusso

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PRIMA/ENGOT-OV26/GOG-3012 STUDY: LONG-TERM CONDITIONAL PFS

#146



Antonio González-Martín,¹ Bhavana Pothuri,² Ignace Vergote,³ Whitney Graybill,⁴ Mansoor R. Mirza,⁵ Colleen C. McCormick,⁶ Domenica Lorusso,⁷ Gilles Freyer,⁸ Floor Backes,⁹ Florian Heitz,¹⁰ Andrés Redondo,¹¹ Richard G. Moore,¹² Christof Vulsteke,¹³ Roisin E. O'Cearbháill,¹⁴ Izabela A. Malinowska,¹⁵ Luda Shtessel,¹⁶ Whitney York,¹⁷ Bradley J. Monk¹⁸

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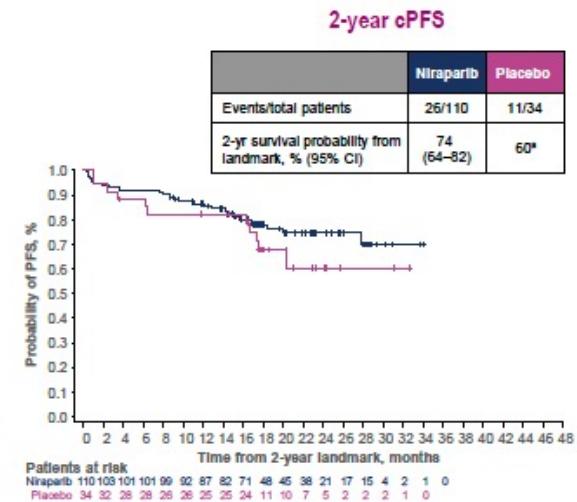
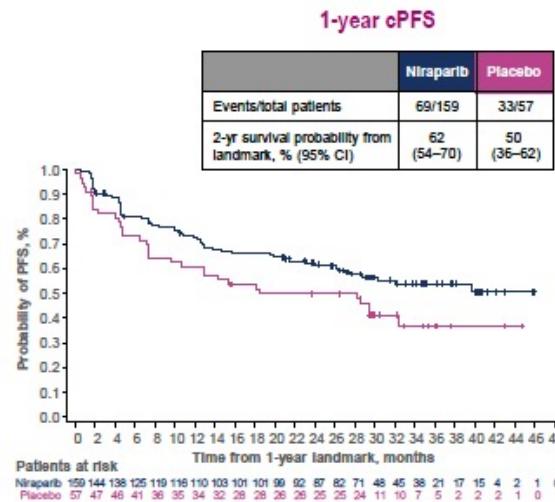
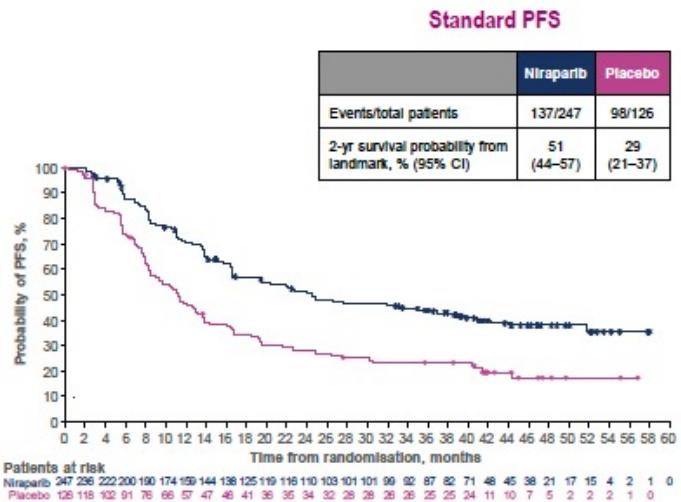
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CONDITIONAL PFS IN THE PRIMA HRd POPULATION



In the HRd population:

- Standard PFS rate at:
 - 3 years was 44% for niraparib and 23% for placebo
 - 4 years was 38% for niraparib and 17% for placebo
- Estimates for cPFS were higher at each additional year of PFS

ESMO GYNAECOLOGICAL CANCERS

Antonio Gonzalez-Martin

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*95% CI were not calculated at time points with <10 patients.
cPFS, conditional progression-free survival; HRd, homologous recombination-deficient; PFS, progression-free survival.



Efficacy of subsequent therapies in patients with advanced ovarian cancer in the Phase III PAOLA-1/ENGOT-ov25 trial according to whether disease progression occurred during or after the end of olaparib maintenance

Philipp Harter,¹ Marie-Ange Mouret-Reynier,² Domenica Lorusso,³ Claire Cropel,⁴ Eva Guerra,⁵ Pia Wolfrum-Ristau,⁶ Takashi Matsumoto,⁷ Ignace Vergote,⁸ Nicoletta Colombo,⁹ Johanna Mäenpää,¹⁰ Coriolan Lebreton,¹¹ Nikolaus de Gregorio,^{12,13} Anna Maria Mosconi,¹⁴ María Jesús Rubio,¹⁵ Hugues Bourgeois,¹⁶ Peter A. Fasching,¹⁷ Anne-Claire Hardy-Bessard,¹⁸ Dominik Denischlag,¹⁹ Eric Pujade-Lauraine,²⁰ Isabelle Ray-Coquard²¹

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Figure 2. Time from first subsequent therapy to second subsequent therapy in patients who received any chemotherapy as first subsequent therapy

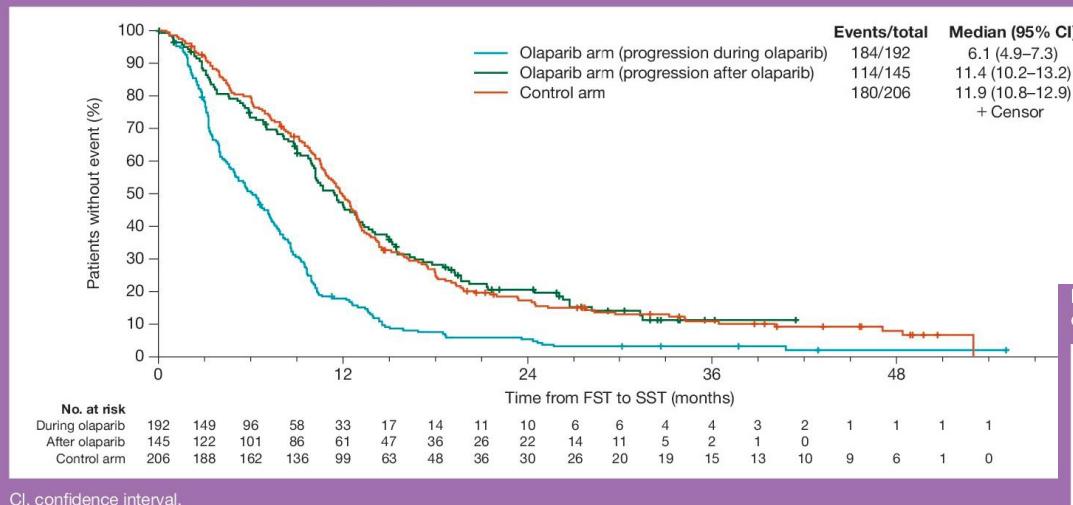
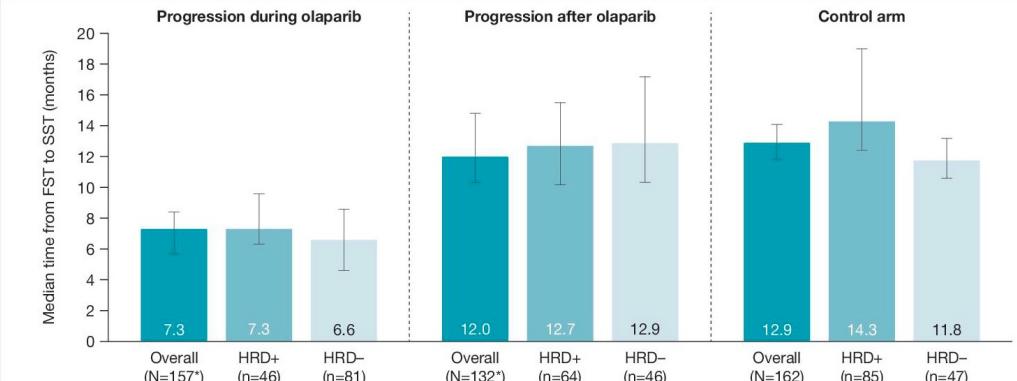


Figure 3. Median time from first subsequent therapy to second subsequent therapy in patients who received a combination therapy including platinum-based chemotherapy as first subsequent therapy



*One patient in the olaparib arm did not receive treatment and was not included in this analysis. Kaplan-Meier estimates with 95% CIs. HRD-positive status was defined as tBRCAm and/or genomic instability score ≥ 42 (Myriad MyChoice HRD Plus assay).



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ANNUAL MEETING

Durvalumab with paclitaxel/carboplatin and bevacizumab followed by maintenance durvalumab, bevacizumab and olaparib in patients with newly diagnosed advanced ovarian cancer without a tumor *BRCA1/BRCA2* mutation: results from the randomized, placebo-controlled Phase III DUO-O/ENGOT-ov46/AGO-OVAR 23/GOG-3025 trial

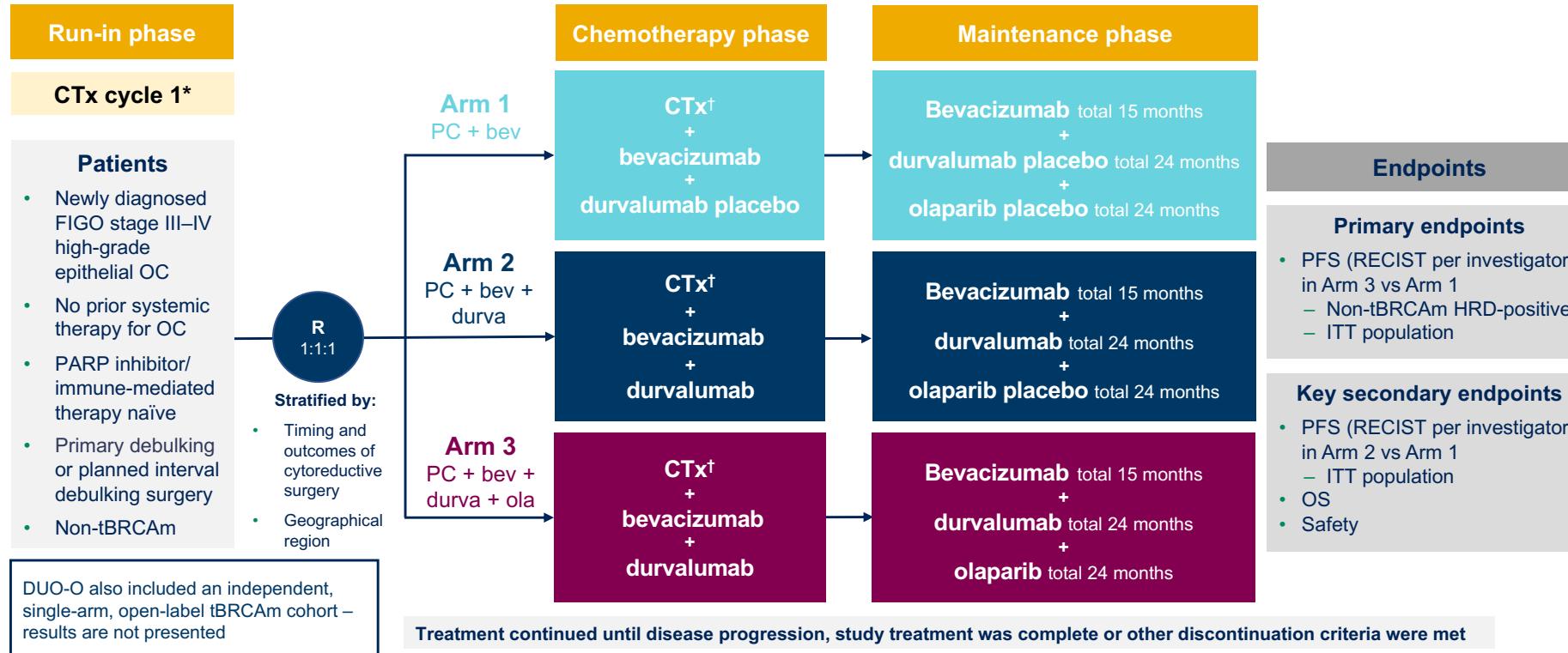
Philipp Harter,¹ Fabian Trillisch,² Aikou Okamoto,³ Alexander Reuss,⁴ Jae-Weon Kim,⁵ Maria Jesús Rubio-Pérez,⁶ Mehmet Ali Vardar,⁷ Giovanni Scambia,⁸ Olivier Trédan,⁹ Gitte-Bettina Nyvang,¹⁰ Nicoletta Colombo,¹¹ Anita Chudecka-Głaz,¹² Christoph Grimm,¹³ Stephanie Lheureux,¹⁴ Els Van Nieuwenhuysen,¹⁵ Florian Heitz,¹⁶ Robert M. Wenham,¹⁷ Kimio Ushijima,¹⁸ Emily Day,¹⁹ Carol Aghajanian²⁰

¹Kliniken Essen-Mitte, Essen, and AGO, Germany; ²University Hospital, LMU Munich, Munich, and AGO, Germany; ³The Jikei University School of Medicine, Tokyo, and JGOG, Japan; ⁴Coordinating Center for Clinical Trials of the Philipps-University of Marburg, Marburg, and ENGOT, Germany; ⁵ Seoul National University Hospital, Seoul, and KGOG, South Korea; ⁶Reina Sofia University Hospital, Cordoba, and GEICO, Spain; ⁷Medical Faculty, University of Cukurova, and Balcali Hospital, Adana, and TRSGO, Turkey; ⁸Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, and MITO, Italy; ⁹Centre Léon Bérard, Centre de Recherche en Cancérologie de Lyon, Lyon, and GINECO, France; ¹⁰Odense Universitetshospital, Odense, and NSGO, Denmark; ¹¹University of Milan-Bicocca and Istituto Europeo di Oncologia IRCCS, Milan, and MANGO, Italy; ¹²SPSK Nr 2, Pomeranian Medical University, Szczecin, and PGOG, Poland; ¹³Gynecologic Cancer Unit, Medical University Vienna, and AGO-Au, Austria; ¹⁴Princess Margaret Hospital, Toronto, ON, and PMHC, Canada; ¹⁵UZ Leuven, Leuven, and BGOG, Belgium; ¹⁶Ev. Kliniken Essen-Mitte, Essen, and Charité Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin Institute of Health, Berlin, and AGO, Germany; ¹⁷Moffitt Cancer Center, Tampa, FL, and GOG-F, USA; ¹⁸Kurume University School of Medicine, Kurume, and JGOG, Japan; ¹⁹Oncology Biometrics, AstraZeneca, Cambridge, UK; ²⁰Memorial Sloan Kettering Cancer Center, New York, NY, and GOG-F, USA

ClinicalTrials.gov identifier: NCT03737643

This study was sponsored by AstraZeneca

DUO-O study design

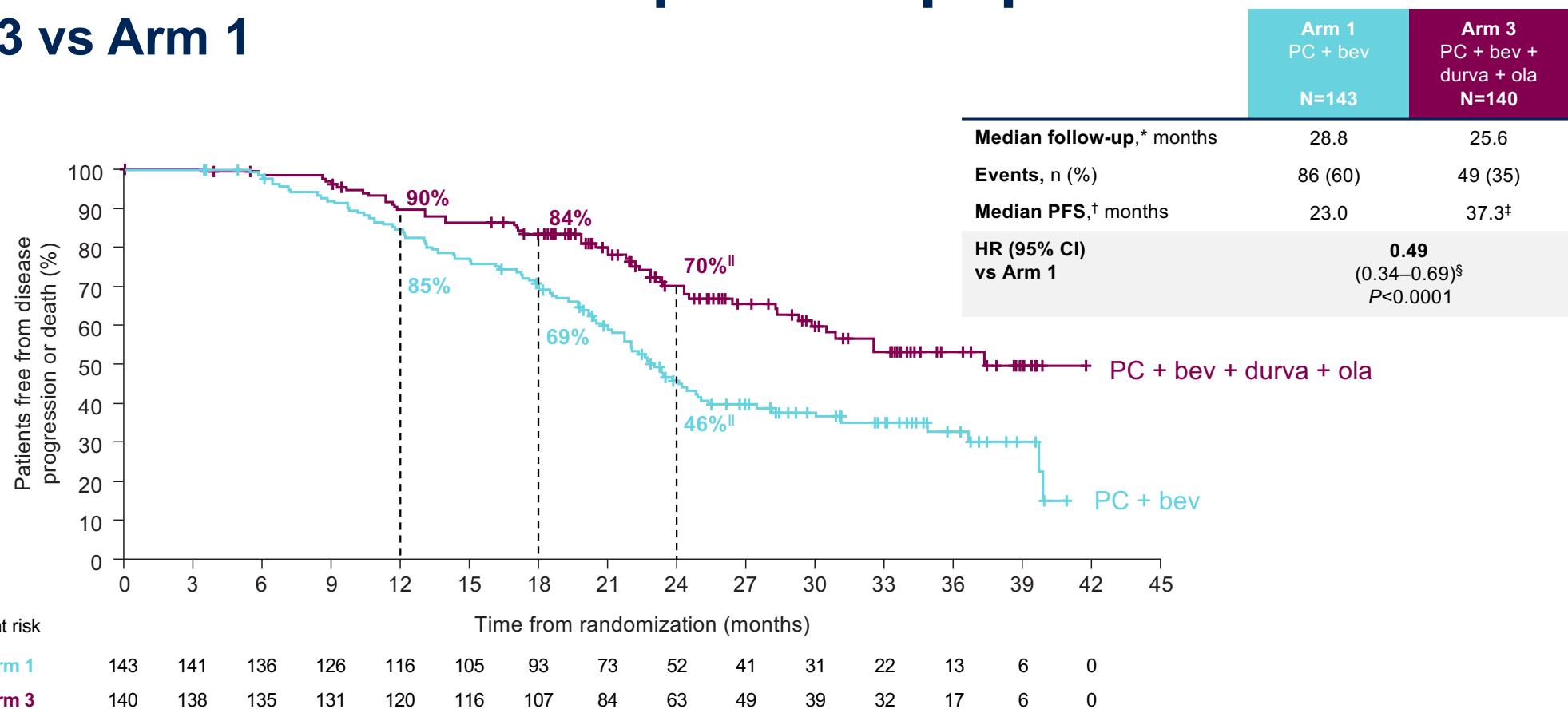


Dosing and schedule: bevacizumab (15 mg/kg IV q3w); durvalumab (1120 mg IV q3w); olaparib (300 mg po bid); chemotherapy: paclitaxel 175 mg/m² IV q3w and carboplatin at AUC5 or AUC6 IV q3w. PFS interim analysis DCO: December 5, 2022.

*With or without bevacizumab according to local practice; †Cycles 2–6; ‡Genomic instability score ≥42 assessed prospectively by Myriad MyChoice CDx assay. AUC, area under the curve; bev, bevacizumab; bid, twice daily; CTx, chemotherapy; DCO, data cutoff; durva, durvalumab; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; ITT, intent-to-treat; IV, intravenous; ola, olaparib; OS, overall survival; PC, paclitaxel/carboplatin; po, by mouth; q3w, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria for Solid Tumors.

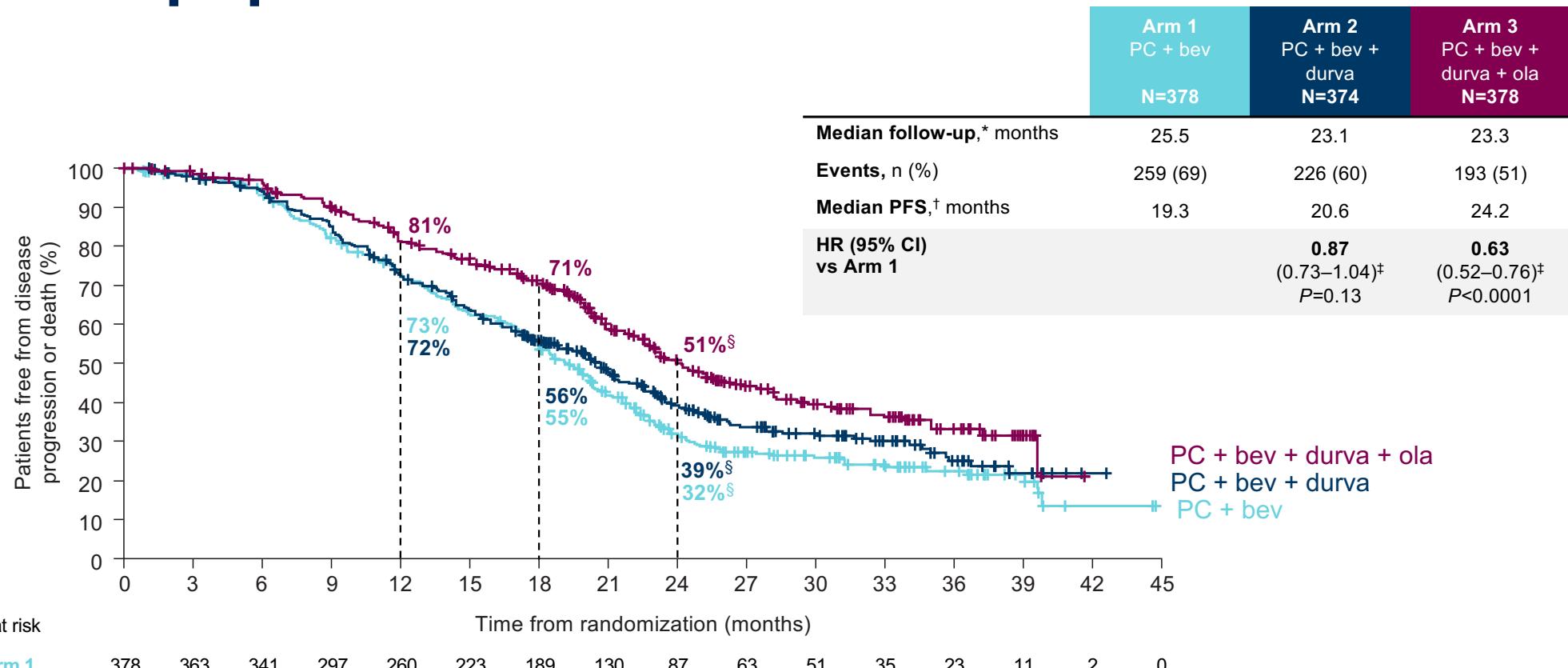
PFS: Non-tBRCAm HRD-positive population

Arm 3 vs Arm 1



*In censored patients; †Medians and rates were estimated by KM method; ‡Median PFS in Arm 3 unstable; §HR and CI were estimated from a stratified Cox proportional hazards model. P value from a stratified log rank test. Model stratified by timing and outcome of cytoreductive surgery; [¶]24-month PFS rates unstable. CI, confidence interval; HR, hazard ratio; KM, Kaplan-Meier.

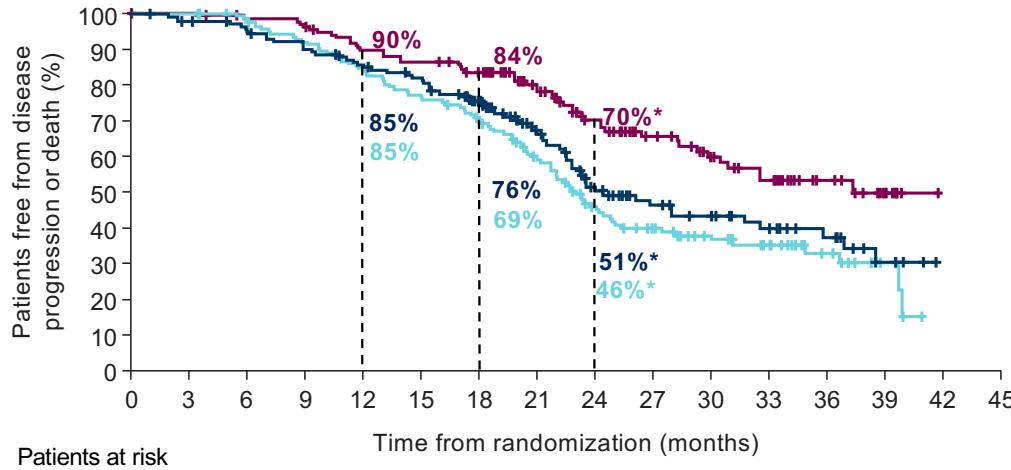
PFS: ITT population



*In censored patients; [†]Medians and rates were estimated by KM method; [‡]HR and CI were estimated from a stratified Cox proportional hazards model. Model stratified by timing and outcome of cytoreductive surgery and geographical region. *P* value from a stratified log rank test; [§]24-month PFS rates unstable.

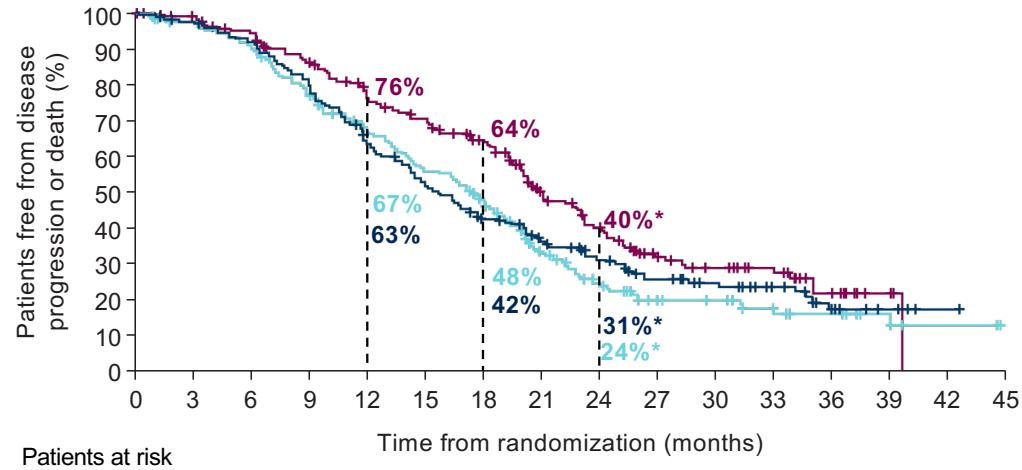
Subgroup analysis of PFS by HRD status

Non-tBRCAm HRD-positive



	Arm 1	Arm 2	Arm 3
PC + bev	143	141	136
N=143	126	116	93
PC + bev + durva	105	73	52
N=148	41	31	22
PC + bev + durva + ola	31	21	13
N=140	13	6	6
0	0	0	0

HRD-negative



	Arm 1	Arm 2	Arm 3
PC + bev	216	203	188
N=216	159	135	112
PC + bev + durva	92	55	34
N=199	34	21	19
PC + bev + durva + ola	21	12	9
N=211	5	2	0
0	0	0	0

	Arm 1 PC + bev N=143	Arm 2 PC + bev + durva N=148	Arm 3 PC + bev + durva + ola N=140
Events, n (%)	86 (60)	69 (47)	49 (35)
Median PFS, months [†]	23.0	24.4 [‡]	37.3 [‡]
HR (95% CI) vs Arm 1	0.82 (0.60–1.12)[§]	0.51 (0.36–0.72)[§]	

	Arm 1 PC + bev N=216	Arm 2 PC + bev + durva N=199	Arm 3 PC + bev + durva + ola N=211
Events, n (%)	157 (73)	142 (71)	127 (60)
Median PFS, months [†]	17.4	15.4	20.9
HR (95% CI) vs Arm 1	0.94 (0.75–1.18)[§]	0.68 (0.54–0.86)[§]	

*24-month PFS rates unstable; [†]Medians and rates were estimated by KM method; [‡]Median PFS in HRD-positive subgroup Arm 3 and Arm 2 unstable; [§]HR and CI were estimated from an unstratified Cox proportional hazards model.



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Atezolizumab combined with platinum-based chemotherapy and maintenance niraparib for recurrent ovarian cancer with a platinum-free interval >6 months: Primary analysis of the double-blind placebo-controlled ENGOT-Ov41/GEICO 69-O/ANITA phase 3 trial

Antonio González-Martín, MD, PhD

Cancer Center Clínica Universidad de Navarra and GEICO, Madrid, Spain

On behalf of MJ Rubio Perez (GEICO, Spain), F Heitz (AGO, Germany), RD Christensen (GEICO & NSGO, Denmark), N Colombo (MaNGO, Italy), T Van Gorp (BGOG, Belgium), A Oaknin (GEICO, Spain), A Leary (GINECO, France), L Gaba (GEICO, Spain), C Lebreton (GINECO, France), LM De Sande González (GEICO, Spain), M Romeo Marin (GEICO, Spain), A Redondo (GEICO, Spain), MP Barretina Ginesta (GEICO, Spain), JA Perez-Fidalgo (GEICO, Spain), A Santaballa Bertran (GEICO, Spain), MJ Bermejo-Pérez (GEICO, Spain), I Bruchim (ISGO, Israel), I Ray-Coquard (GINECO, France), F Selle (GINECO, France)

LBA37, Madrid, Spain, 20th October 2023

ANITA = Atezolizumab and Niraparib Treatment Association

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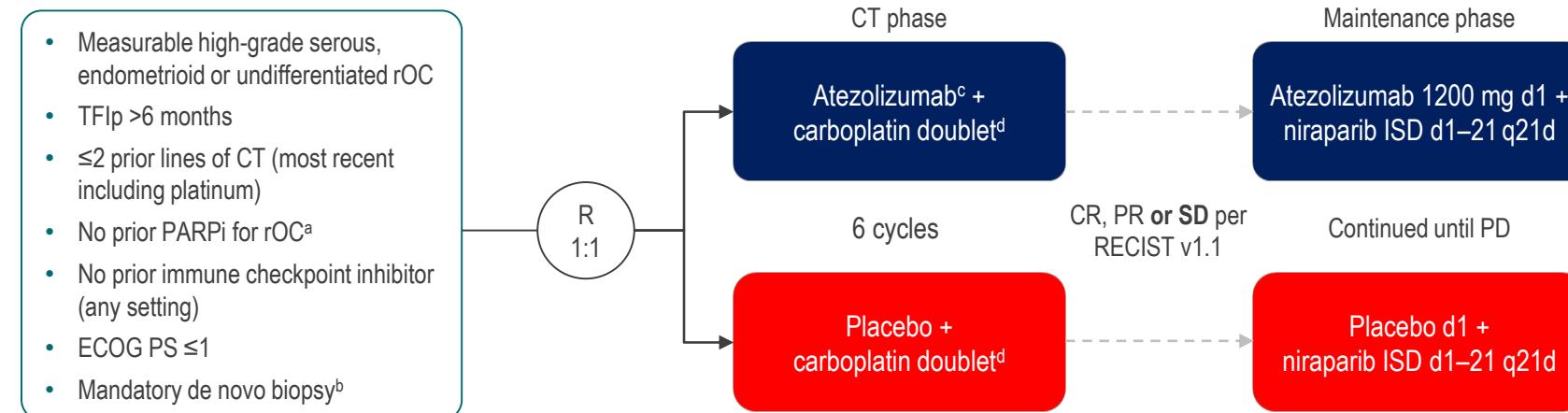
ENGOT
European Network of
Gynaecological Oncological Trial groups





ANITA/ENGOT-Ov41/GEICO 69-O (NCT03598270) trial design

Placebo-controlled multicentre randomised phase 3 trial



Stratification factors:

- Carboplatin doublet (PLD vs gemcitabine vs paclitaxel)
- TFIp (6–12 vs >12 months)
- BRCA status (mutated vs non-mutated)
- PD-L1 status (IC <1% vs ≥1% vs non-informative)^e

AUC = area under the curve; CR = complete response; d = day; ECOG PS = Eastern Cooperative Oncology Group performance status; IC = immune cells; ISD = individualised starting dose (300 mg, or 200 mg if baseline weight is <77 kg or baseline platelet count is <150,000 µL); PD = progressive disease; PLD = pegylated liposomal doxorubicin; PR = partial response; q21d = every 21 days; R = randomisation; RECIST = Response Evaluation Criteria in Solid Tumours; SD = stable disease

^aPrior PARPi after front-line therapy permitted if continued for ≥18 months (BRCA mutated) or ≥12 months (BRCA wildtype).

^bImplemented after randomisation of 82 patients (whose PD-L1 status was analysed in archival tissue).

^cAtezolizumab 1200 mg d1 q21d or 840 mg d1&8 q28d, depending on CT regimen. ^dCarboplatin AUC5 d1 + paclitaxel 175 mg/m² d1 q21d OR carboplatin AUC4 d1 + gemcitabine 1000 mg/m² d1&8 q21d OR carboplatin AUC5 d1 + PLD 30 mg/m² d1 q28d.

^ePD-L1-expressing IC on tumour area, determined by SP142 assay. Non-informative cases were capped at <10%



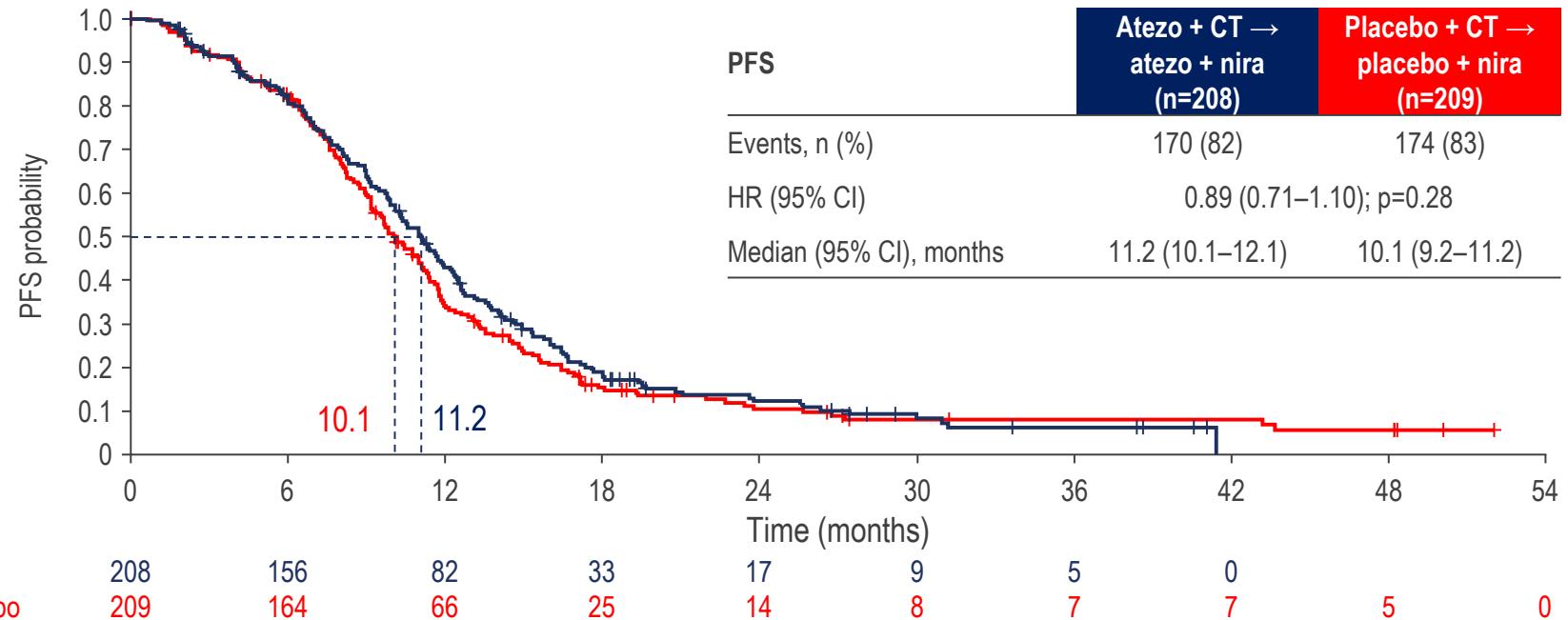
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Primary endpoint: PFS



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DOI: 10.18637/hitos.2023.001



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Poster 795P

Tolerability and effectiveness of niraparib in long-term responders with platinum-sensitive recurrent ovarian cancer (GEICO-88R study)

Juan F. Cueva, Carmen Salvador, Fernando Gálvez, Josefa Ferreiro Quintana, Sara Cros, Santiago González-Santiago, Javier Cassinello, Margarita Romeo, Piedad Reche, Mariam Soriano, María Valero Arbizu, M^a Jesús Rubio, Martín Oré-Arce, Lydia Gaba, M^a del Mar Gordón, César Gómez-Raposo, Susana Hernando, Raúl Márquez, José Fuentes, Antonio González-Martín

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INTRODUCTION

The GEICO-88R study assessed the real-world use of niraparib as maintenance treatment in patients (pts) with platinum-sensitive recurrent high-grade ovarian cancer (OC) within the Spanish expanded access program (1). A preplanned sub-analysis of long-term responders (LTR) is presented. The data cutoff date is June 22, 2022, and it includes information on 107 LTR patients and 209 non-LTR patients.

OBJECTIVE

To evaluate the tolerability and effectiveness of niraparib in the LTR sub-population, including an assessment of patient characteristics and niraparib dosing.

A specific assessment of LTR to niraparib maintenance treatment (exposure ≥ 12 months) was performed, describing patient characteristics, niraparib dosing, tolerability, and effectiveness. To complete the information, we also reviewed the complementary population of the pivotal study, non-long-term responders (NLTR).



RESULTS

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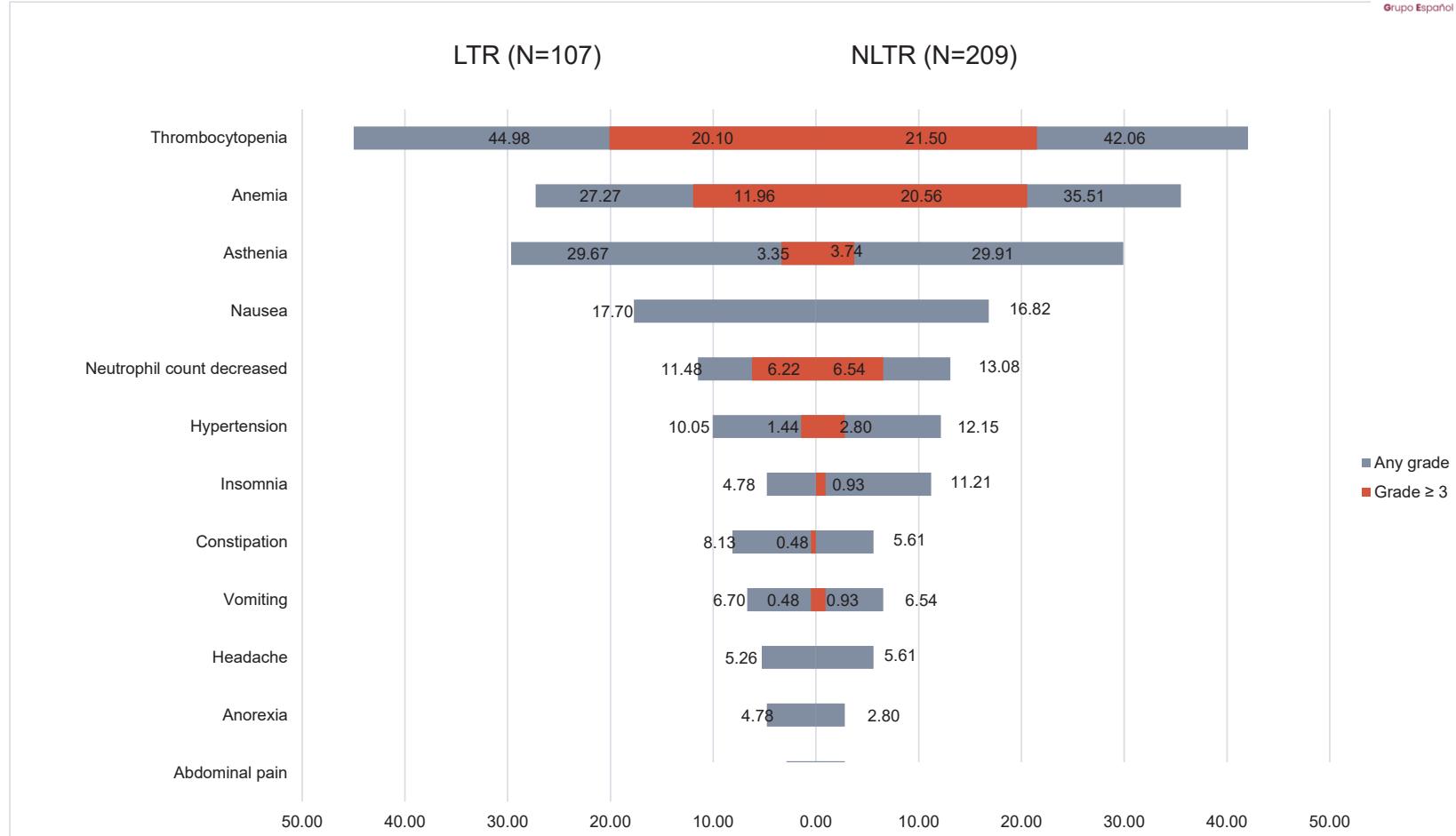
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Figure 1. Niraparib toxicities



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Figure 2. Long-term responders mPFS (27.2 mo)
Median follow-up 29.95 months

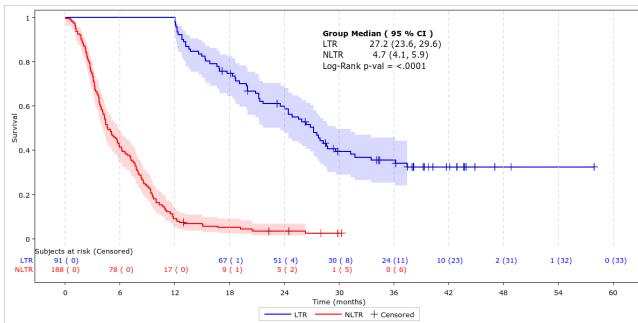


Figure 3. Long-term responders PFS2 (42.3 mo)

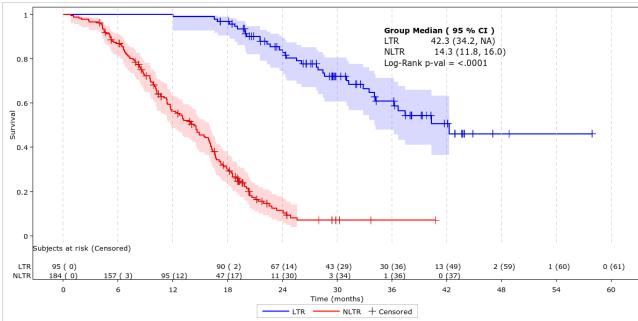
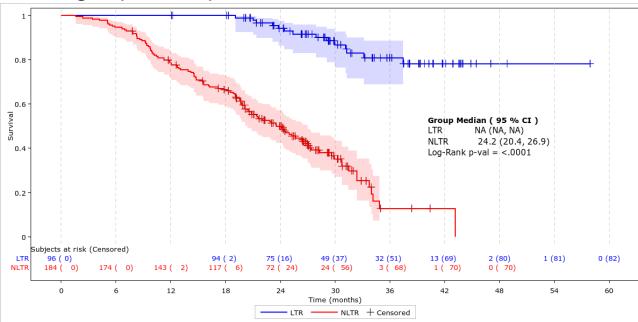


Figure 4. Long-term responders OS
LTR group 85.4% pts alive



A long treatment duration (more than 24 months) was achieved in more than 50% of LTR patients, with a good tolerability profile, in a real-world setting.

Moreover, despite their high-risk characteristics, PFS2 and OS results are good, suggesting effectiveness of subsequent treatments.



The most common Grade ≥3 TEAEs associated with PARPi monotherapy are haematologic

	PRIMA ¹ Niraparib (n=484)	PRIME ² Niraparib (n=255)	SOLO1 ³ Olaparib (n=260)	PAOLA-1 ⁴ Olaparib + bev (n=535)		ATHENA-MONO ⁵ Rucaparib (n=427)
Any grade AEs, %	99	99	98	99	96	97
Grade 3 AEs, %	70	55	39	57	51	61
	Anaemia (31)	Anaemia (18)	Anaemia (22)	Hypertension (19)	Hypertension (30)	Anaemia [†] (29)
	Thrombocytopenia (29)	Neutrophil count decrease [‡] (17)	Neutropenia (9)	Anaemia (17)	Neutropenia (3)	Neutropenia (15)
Most common Grade ≥3 AEs (%)	Platelet count decrease (13)	Platelet count decrease [§] (14)	Fatigue (4)	Lymphopenia (7)	Vomiting (2)	ALT/AST increase (11)
	Neutropenia (13)	White blood cell count decrease ^{**} (7)	Diarrhoea (3)	Neutropenia (6)	Abdominal pain (2)	Thrombocytopenia (7)
	Fatigue (2)	GGT increase (5)	Abdominal pain (2)	Fatigue (5)	Diarrhoea (2)	Asthenia/fatigue (5)
Dose interruptions due to AEs, %	80	63	52	54	24	61
Dose reductions due to AEs, %	71	40	28	41	7	49
Discontinuations due to AEs, %	12	7	12	20	6	12

1. González-Martin A, et al. N Engl J Med 2019;381:2391–402; 2. Li N, et al. presented at SGO 2022, 18–21 Mar, Phoenix, AZ; 3. Moore KN, et al. N Engl J Med 2018;379:2495–505; 4. Ray-Coquard I, et al. N Engl J Med 2019;381:2416–28; 5. Monk BJ, et al. J Clin Oncol 2022; <https://doi.org/10.1200/JCO.22.01003>.



Clinical Risk Probably Isn't Enough

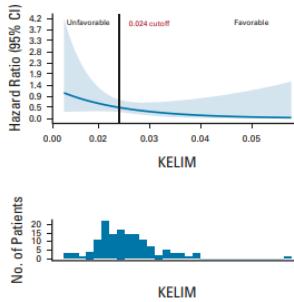
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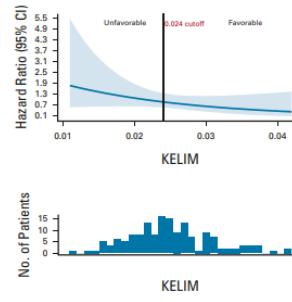
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KELIM

*BRCA*mut in VELIA



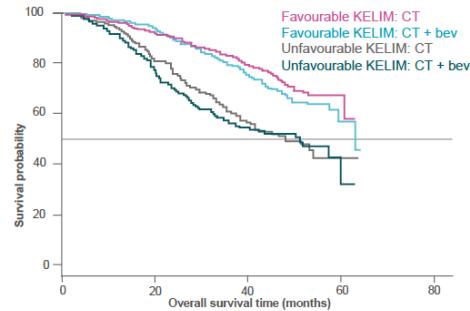
*BRCA*wt/HRD in VELIA



KELIM high correlated with higher chemosensitivity and higher efficacy of veliparib in HRD; KELIM low correlated with poor chemosensitivity and limited efficacy of veliparib in patients with *BRCA*mut tumors or HRD

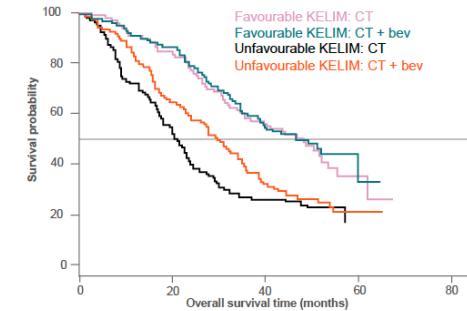
KELIM & bevacizumab benefit in ICON-7

OS in patients with low-risk disease



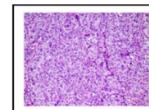
Unfavorable KELIM	<1.0
Favorable KELIM	≥1.0

OS in patients with high-risk disease



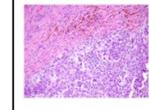
Chemosensitivity, as assessed by KELIM, may be a complementary covariate to consider for decision-making about bevacizumab prescription. Approximately 47% of high-risk patients may not derive survival benefit from the addition of bevacizumab, however, the remaining 53% patients with poorly chemo-sensitive diseases may achieve the maximum survival gain of approximately 9 months.

CRS: Chemotherapy Response Score



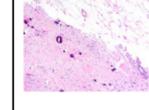
CRS 1

No or minimal tumor response. Mainly viable tumor with no or minimal regression-associated fibroinflammatory changes, limited to a few foci; cases in which it is difficult to decide between regression and tumor-associated desmoplasia or inflammatory cell infiltration.



CRS 2

Appreciable tumor response amid viable tumor that is readily identifiable. Tumor is regularly distributed, ranging from multifocal or diffuse regression-associated fibroinflammatory changes with viable tumor in sheets, streaks, or nodules to extensive regression-associated fibroinflammatory changes with multifocal residual tumor, which is easily identifiable.



CRS 3

Complete or near-complete response with no residual tumor or minimal, irregularly scattered tumor foci seen as individual cells, cell groups or nodules up to 2 mm maximum size. Mainly regression-associated fibroinflammatory changes or very little residual tumor in the complete absence of any inflammatory response.

1. Lawson BC, et al. A 3-Tier Chemotherapy Response Score for Ovarian/Fallopian Tube/Peritoneal High-grade Serous Carcinoma: Is it Clinically Relevant?. The American Journal of Surgical Pathology: February 2020. Ergasti R. *BRCA* status and platinum sensitivity in advanced ovarian cancer according to Chemotherapy Response Score. Int J Gynecol Cancer. 2022 May 3;32(5):639-645; 2. Alvarez Secord A. Predictive Blood-Based Biomarkers in Patients with Epithelial Ovarian Cancer Treated with Carboplatin and Paclitaxel with or without Bevacizumab: Results from GOG-0218. Clin Cancer Res. 2020 Mar 15;26(6):1288-1296; 3. Colombar O. Bevacizumab for Newly Diagnosed Ovarian Cancers: Best Candidates Among High-Risk Disease Patients (ICON-7). JNCI Cancer Spectr. 2020 Apr 4;4(3).



CONSLUSIONS



Maintenance is standard of care in ALL newly diagnosed advanced ovarian cancer

- Maintenance therapy with PARPis has demonstrated clinically meaningful improvements in PFS/OS in newly diagnosed advanced OC, with the greatest benefit in patients with HRd tumours.
- Pts. With BRCA_{mut} tumors **must** receive a PARPi.
- Benefit of BEV added to PARPi in pts. With BRCA_{mut} __> deserves further research.
- Pts. With HRD/BRCA_{wt} **must** receive a PARPi alone or in combination with Bevacizumab.
- Pts. With HRp __> **PARPi or Bev.**