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Gynecologic Malignancies: New Therapeutic Developments

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Discussion Outline

- Review what is new in ovarian cancer
- Review what is new in uterine cancer
- Review what is new in cervical (vaginal & vulvar) cancers

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2023 ASCO ANNUAL MEETING

DESTINY-PanTumor02

Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: DESTINY-PanTumor02 interim results

Funda Meric-Bernstam

The University of Texas MD Anderson Cancer Center, Houston, TX, USA

June 5, 2023

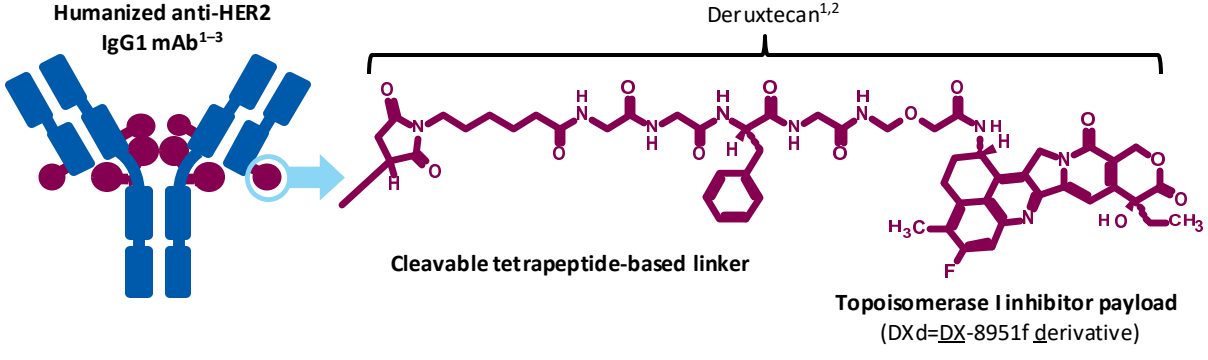
Additional authors: Vicky Makker, Ana Oaknin, Do-Youn Oh, Susana Banerjee, Antonio González-Martín, Kyung Hae Jung, Iwona Ługowska, Luis Manso, Aránzazu Manzano, Bohuslav Melichar, Salvatore Siena, Daniil Stroyakovskiy, Chiedozie Anoka, Yan Ma, Soham Puvvada, Jung-Yun Lee

On behalf of the DESTINY-PanTumor02 investigators

Trastuzumab Deruxtecan (T-DXd) was Designed with Seven Key Attributes

T-DXd is an ADC with three components:

1. A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
2. A topoisomerase I inhibitor payload, an exatecan derivative
3. A tetrapeptide-based cleavable linker



Seven Key Attributes[a,1–5]
Payload mechanism of action: topoisomerase I inhibitor
High potency of payload
High drug-to-antibody ratio ≈8
Payload with short systemic half-life
Stable linker payload
Tumor-selective cleavable linker
Bystander antitumor effect

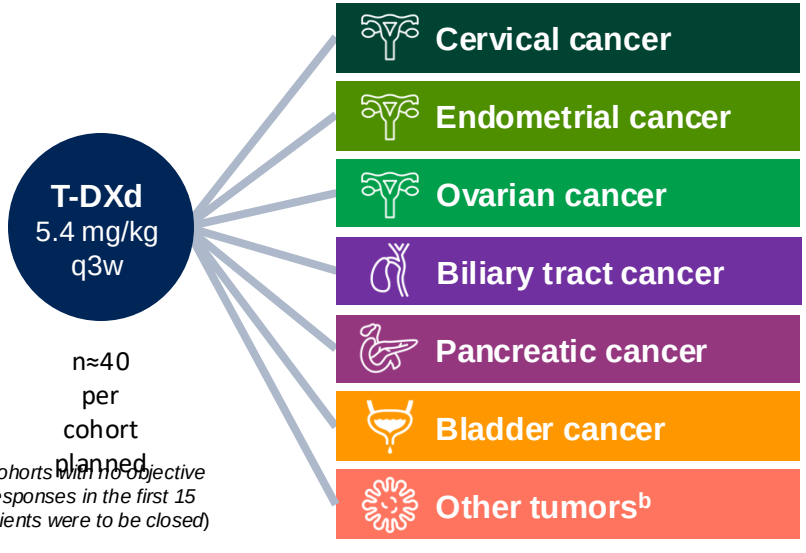
[a]The clinical relevance of these features is under investigation.

ADC, antibody–drug conjugate; HER2, human epidermal growth factor receptor 2; IgG1, immunoglobulin G1; mAb, monoclonal antibody; T-DXd, trastuzumab deruxtecan.
1. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173–185. 2. Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097–5108. 3. Trail PA, et al. *Pharmacol Ther*. 2018;181:126–142.
4. Okamoto H, et al. *Xenobiotica*. 2020;50(10):1242–1250. 5. Nagai Y, et al. *Xenobiotica*. 2019;49(9):1086–1096.

DESTINY-PanTumor02: A Phase 2 Study of T-DXd for HER2-Expressing Solid Tumors

An open-label, multicenter study (NCT04482309)

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer guidelines[1])[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1



Primary endpoint

- Confirmed ORR (investigator)[c]

Secondary endpoints

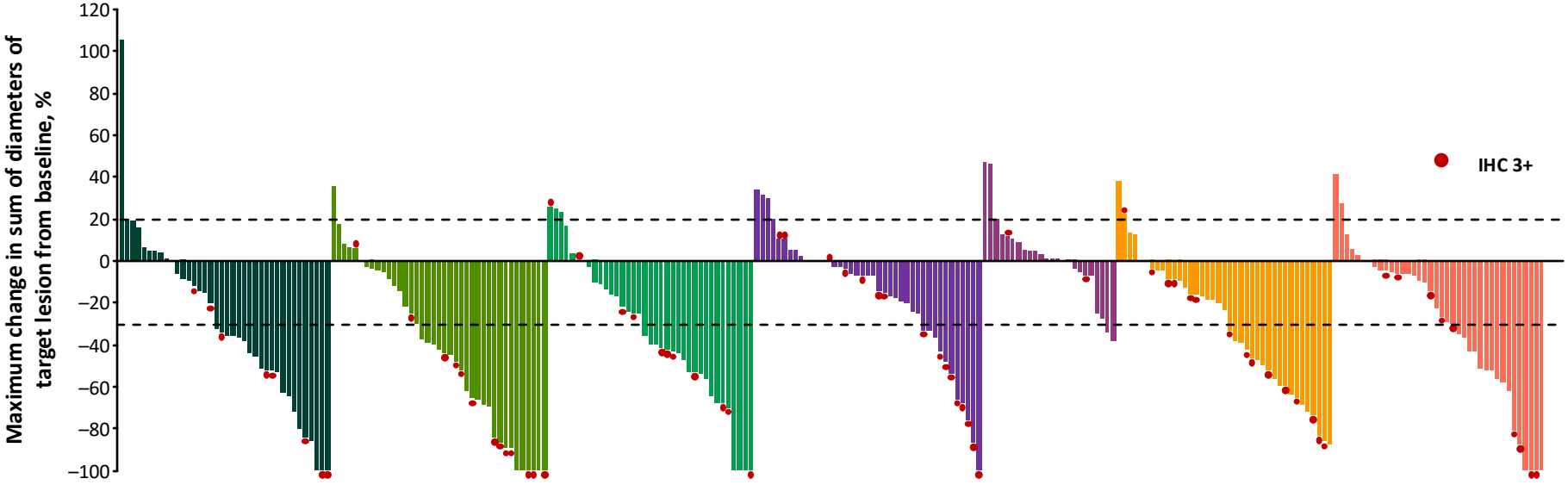
- DOR[c]
- DCR[c]
- PFS[c]
- OS
- Safety

Data cut-off for analysis:

- Nov 16, 2022

[a]Patients were eligible for either test. All patients were centrally confirmed. [b]Patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer.
[c]Investigator-assessed per Response Evaluation Criteria In Solid Tumors version 1.1.
2L, second-line; ASCO, American Society of Clinical Oncology; DCR, disease control rate; CAP, College of American Pathologists; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2;
IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization.
1. Hofmann M, et al. *Histopathology 2008*;52(7):797–805.

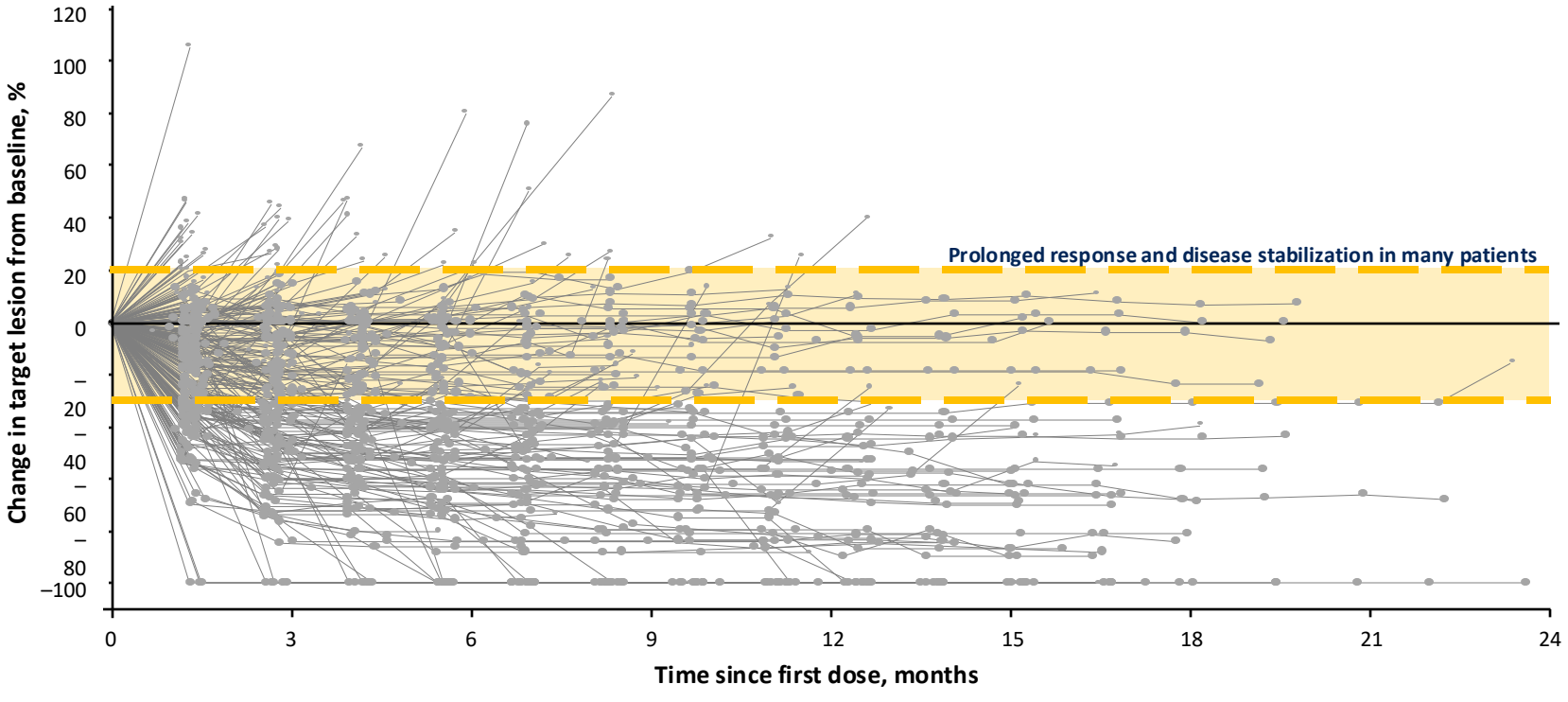
Best Percentage Change in Target Lesion From Baseline



ORR in IHC 3+	Cervical (n=8)	Endometrial (n=13)	Ovarian (n=11)	BTC (n=16)	Pancreatic (n=2)	Bladder (n=16)	Other[a] (n=9)
n (%)	6 (75.0)	11 (84.6)	7 (63.6)	9 (56.3)	0	9 (56.3)	4 (44.4)

Analyses were performed in patients who received ≥1 dose of T-DXd (n=267). Analysis of ORR in IHC 3+ was performed in patients with centrally confirmed HER2 status (n=75).
[a]Responses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer.
BTC, biliary tract cancer; IHC, immunohistochemistry; ORR, objective response rate.

Percentage Change in Target Lesions Over Time



Analyses were performed in patients who received ≥1 dose of T-DXd (n=267).

- ORR: 37.1% (61.3% in patients with IHC 3+)
- Median DOR: 11.8 m (22.1m in patients with IHC 3+)
- Safety of T-DXd was consistent with the known profile

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Ovarian cancer

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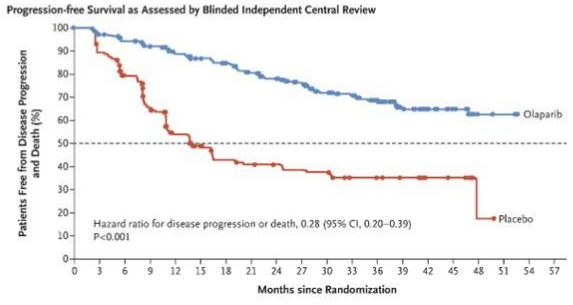
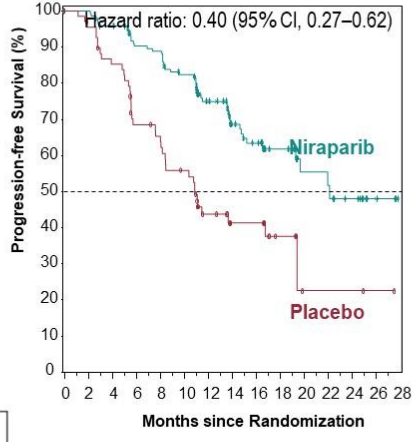
BRCA1/2 mutations remain our BEST biomarker for PARPi benefit accross 1st line trials

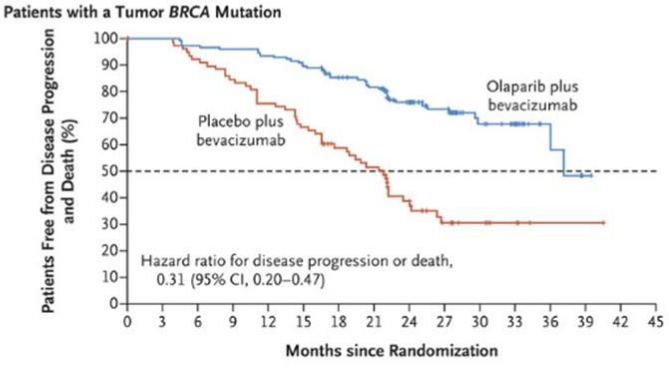
SOLO1



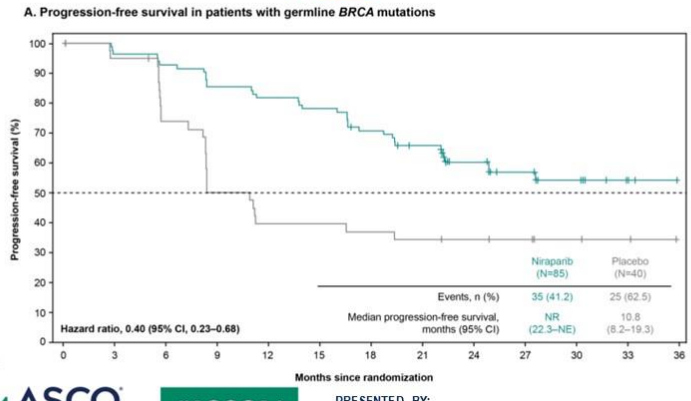
PRIMA



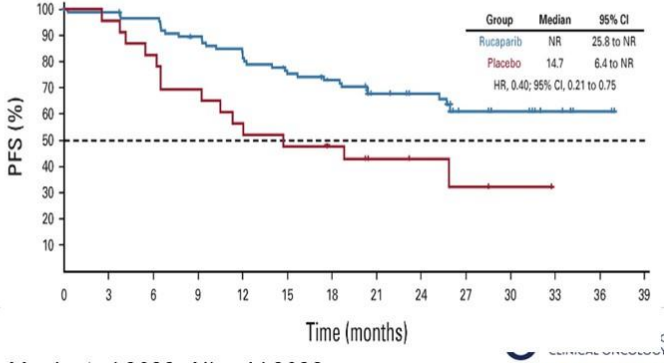
PAOLA



PRIME



ATHENA



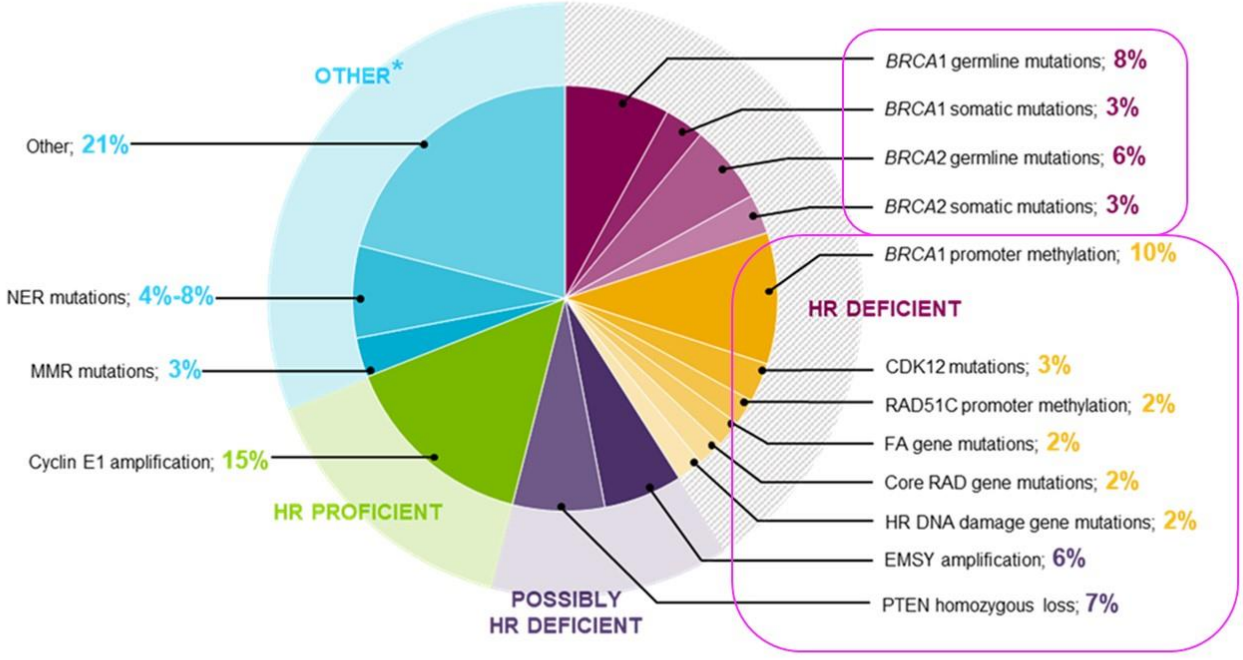
2024 ASCO ANNUAL MEETING #ASCO24

PRESENTED BY:

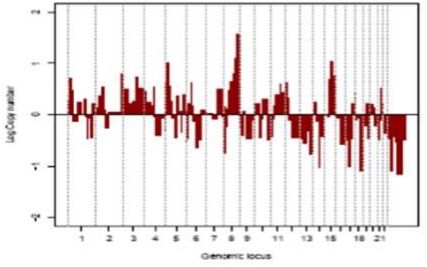
Moore et al 2018, Gonzalez-Martin et al 2019, Ray-Coquard et al 2019, Monk et al 2022, Ning Li 2023

E CONQUERS CANCER

What we have learned… Beyond BRCAm OC, a further subset likely homologous recombination deficient (HRD)



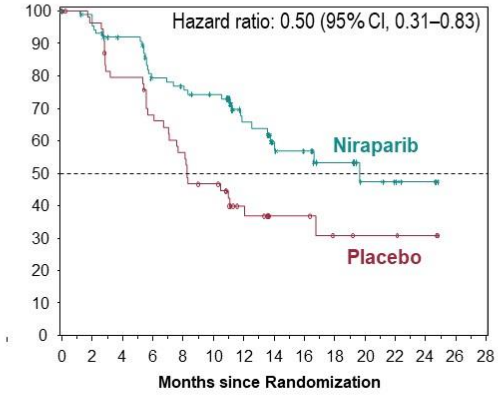
What characterizes HRD-positive OC = high levels of genomic instability



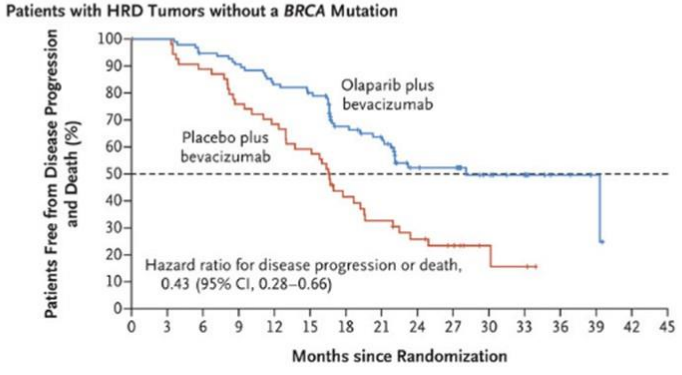
poulos et al. Cancer Discov. 2015

High genomic instability score (GIS) is our 2nd best biomarker to select patients for PARPi – 1st line trials

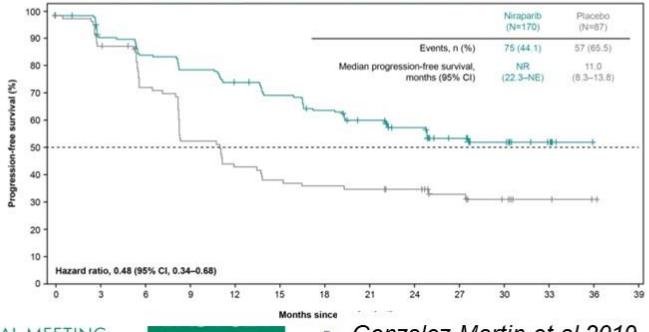
PRIMA, BRCAwt/GIS+



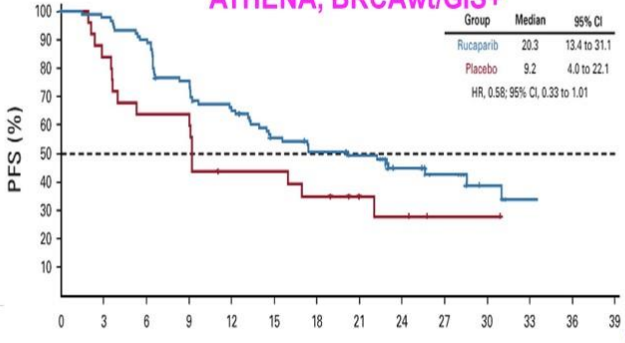
PAOLA, BRCAwt/GIS+



PRIME, BRCAm or BRCAwt/GIS+



ATHENA, BRCAwt/GIS+



Gonzalez-Martin et al 2019, Ray-Coquard et al 2019, Monk et al 2022, Ning Li 2023

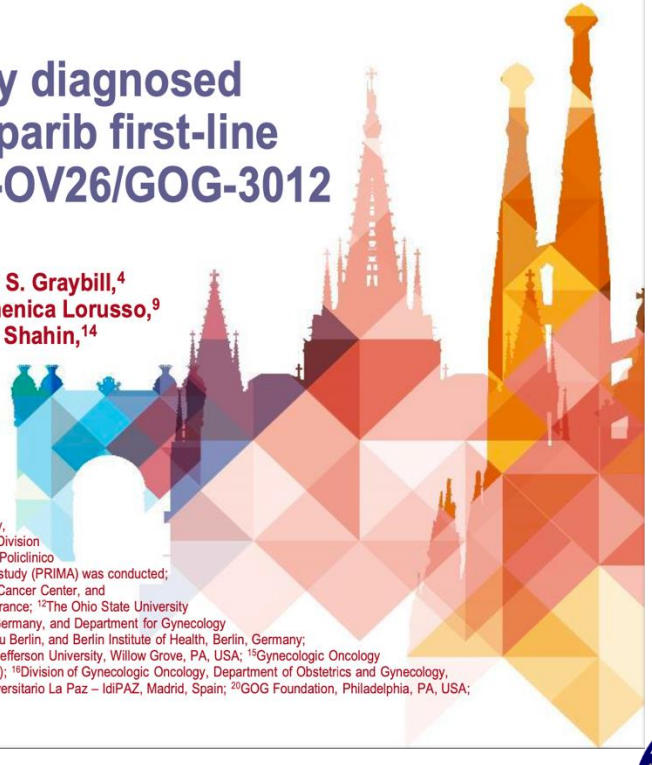
BARCELONA 2024 ESMO congress

Final overall survival in patients with newly diagnosed advanced ovarian cancer treated with niraparib first-line maintenance: results from PRIMA/ENGOT-OV26/GOG-3012

Presentation LBA29

Antonio González-Martín,[1] Bhavana Pothuri,[2] Maria Pilar Barretina-Ginesta,[3] Whitney S. Graybill,[4] Ignace Vergote,[5] Colleen C. McCormick,[6] Mansoor R. Mirza,[7] Richard G. Moore,[8] Domenica Lorusso,[9] Roisin E. O'Cearbhaill,[10] Gilles Freyer,[11] David. M. O'Malley,[12] Florian Heitz,[13] Mark S. Shahin,[14] Ilan Bruchim,[15] William H. Bradley,[16] Natalie Compton,[17] Izabela A. Malinowska,[18] Andrés Redondo,[19] Bradley J. Monk[20]

[1]Medical Oncology Department, Translational Oncology Group, CIMA, Universidad de Navarra, Cancer Center Clínica Universidad de Navarra, and Grupo Español de Investigación en Cáncer ginecológicO (GEICO), Madrid, Spain; [2]Gynecologic Oncology Group (GOG) Foundation and Departments of Obstetrics/Gynecology and Medicine, Division of Gynecologic Oncology, Laura & Isaac Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA; [3]Medical Oncology Department, Institut Català d'Oncologia, Girona Biomedical Research Institute (IDIBGI-CERCA), Girona University, Girona, Spain, and GEICO, Spain; [4]Division of Gynecologic Oncology, Medical University of South Carolina, Charleston, SC, USA; [5]University Hospitals Leuven, Leuven Cancer Institute, and Belgium and Luxembourg Gynaecological Oncology Group (BGOG), Leuven, Belgium; [6]Legacy Medical Group Gynecologic Oncology, Portland, OR, USA, when the analysis was conducted; present affiliation, John Hopkins Hospital, Baltimore, MD, USA; [7]Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, and Nordic Society of Gynaecologic Oncology-Clinical Trial Unit, Copenhagen, Denmark; [8]Division of Gynecologic Oncology, Wilmot Cancer Institute, Department of Obstetrics and Gynecology, University of Rochester, Rochester, NY, USA; [9]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Catholic University of Sacred Heart, and Multicenter Italian Trials in Ovarian Cancer (MITO), Rome, Italy, when the study (PRIMA) was conducted; present affiliation, Humanitas San Pio X, Milan, Humanitas University, Pieve Emanuele (Milan), Italy; [10]Department of Medicine, Memorial Sloan Kettering Cancer Center, and Weill Cornell Medical College, New York, NY, USA, and GOG Foundation; [11]Centre Hospitalier Lyon-Sud Hospices Civils de Lyon, Oullins-Pierre-Bénite, France; [12]The Ohio State University and James Comprehensive Cancer Center, Columbus, OH, USA; [13]Department of Gynecology and Gynecologic Oncology, Kliniken Essen-Mitte, Essen, Germany, and Department for Gynecology with the Center for the Oncologic Surgery Charité Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany; [14]Hanjani Institute for Gynecologic Oncology, Abington Hospital–Jefferson Health, Asplundh Cancer Pavilion, Sidney Kimmel Medical College of Thomas Jefferson University, Willow Grove, PA, USA; [15]Gynecologic Oncology Department, Hillel Yaffe Medical Center, Hadera, Israel, Technion Institute of Technology, Haifa, Israel and Israeli Society of Gynecologic Oncology (ISGO); [16]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Medical College of Wisconsin, Milwaukee, WI, USA; [17]Compton Statistical Consulting Limited, Westerham, UK; [18]GSK, Waltham, MA, USA; [19]Hospital Universitario La Paz – IdiPAZ, Madrid, Spain; [20]GOG Foundation, Philadelphia, PA, USA; Florida Cancer Specialists and Research Institute, West Palm Beach, FL, USA.



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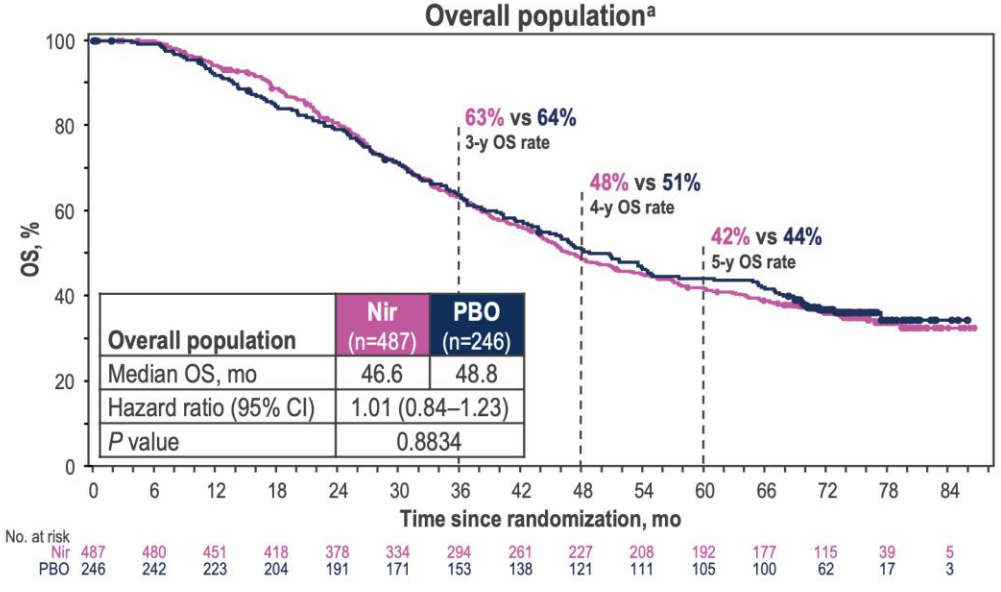
Final OS (62.5% maturity in overall population)

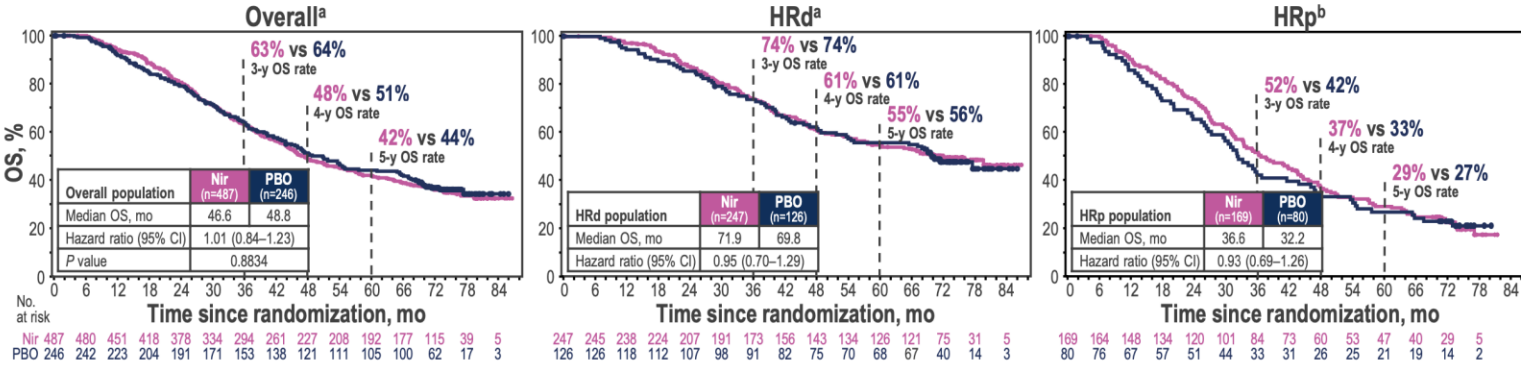
No difference in OS between niraparib and placebo arms



[a]Results for overall population evaluated with stratified log-rank test. Hazard ratio and 95% CI calculated using stratified Cox proportional hazards model with randomization stratification factors. Nir, niraparib; OS, overall survival; PBO, placebo.

Final OS (62.5% maturity in overall population)

No difference in OS between niraparib and placebo arms in the overall, HRd, and HRp populations

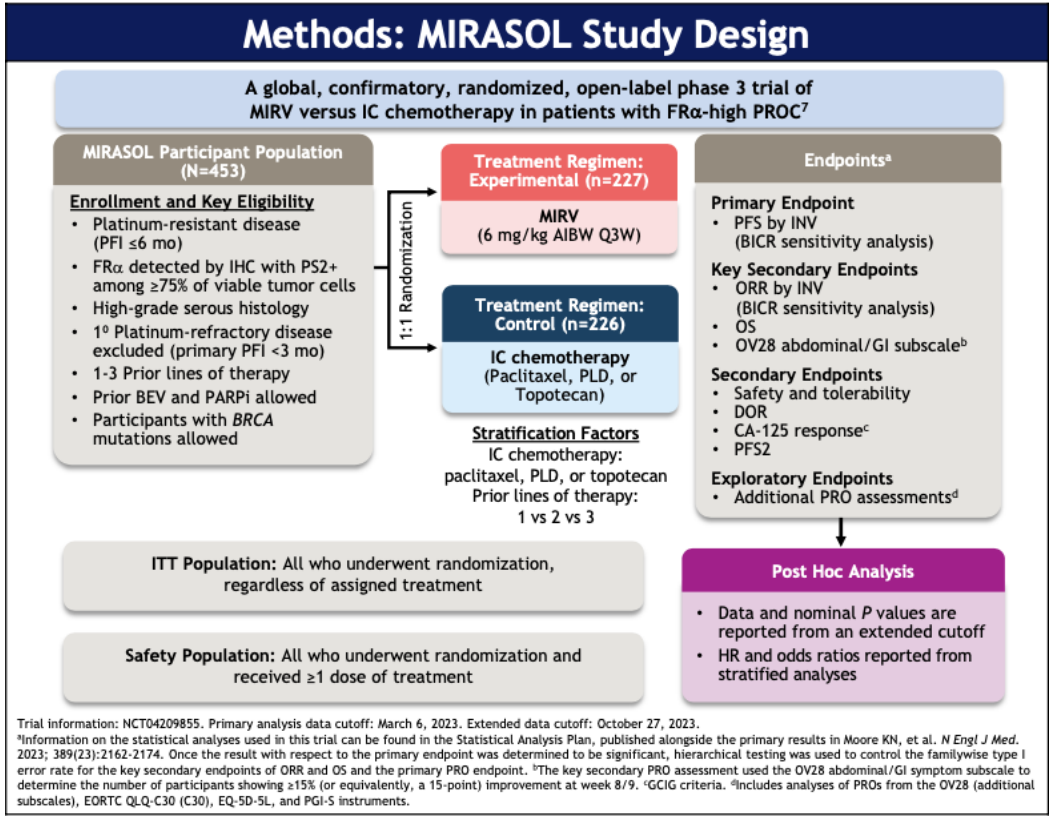


- OS results for all prespecified biomarker-defined subgroups consistent with overall population[c]

[a]Hazard ratios and 95% CIs for overall and HRd populations calculated using stratified Cox proportional hazards model with randomization stratification factors. [b]Hazard ratio and 95% CI for HRp population calculated using unstratified Cox proportional hazards model. [c]OS results for the HRnd population (unstratified): hazard ratio (95% CI), 1.39 (0.88–2.19). aOC, advanced ovarian cancer; HRd, homologous recombination deficient; HRnd, homologous recombination status not determined; HRp, homologous recombination proficient; OS, overall survival; Nir, niraparib; PBO, placebo.

1. Matulonis UA, et al. *Cancer*. 2015;121(11):1737–1746. 2. Siegel RL, et al. *CA Cancer J Clin*. 2024;74(1):12–49. 3. Elattar A, et al. *Cochrane Database Syst Rev*. 2011;201(8):CD007565. 4. Sun C, et al. *PLoS One*. 2014;9(5):e95285. 5. Delgado A, et al. *Am J Cancer Res*. 2021;11(4):1121–1131.

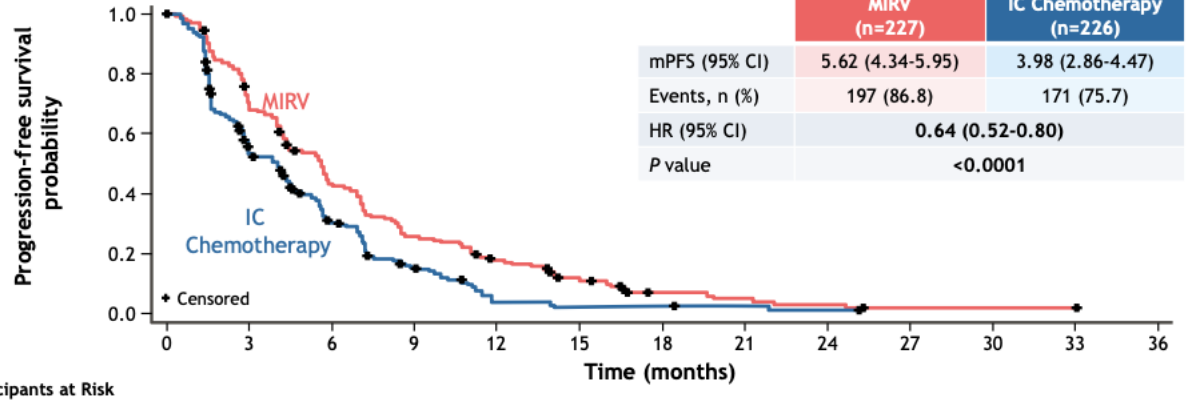
Methods: MIRASOL Study Design



Trial information: NCT04209855. Primary analysis data cutoff: March 6, 2023. Extended data cutoff: October 27, 2023.
[a]Information on the statistical analyses used in this trial can be found in the Statistical Analysis Plan, published alongside the primary results in Moore KN, et al. *N Engl J Med*. 2023; 389(23):2162-2174. Once the result with respect to the primary endpoint was determined to be significant, hierarchical testing was used to control the familywise type I error rate for the key secondary endpoints of ORR and OS and the primary PRO endpoint. [b]The key secondary PRO assessment used the OV28 abdominal/GI symptom subscale to determine the number of participants showing ≥15% (or equivalently, a 15-point) improvement at week 8/9. [c]GCIG criteria. [d]Includes analyses of PROs from the OV28 (additional subscales), EORTC QLQ-C30 (C30), EQ-5D-5L, and PGI-S instruments.

Results: Updated Progression-Free Survival in MIRASOL

Figure 1. Post Hoc Progression-Free Survival by Investigator[a]



	MIRV (n=227)	IC Chemotherapy (n=226)
mPFS (95% CI)	5.62 (4.34-5.95)	3.98 (2.86-4.47)
Events, n (%)	197 (86.8)	171 (75.7)
HR (95% CI)	0.64 (0.52-0.80)	
P value	<0.0001	

No. of Participants at Risk

MIRV	227	151	89	53	35	19	7	5	3	1	1	1	0
IC Chemotherapy	226	98	49	22	5	3	3	2	1	0			

Extended data cutoff: October 27, 2023.
[a]Intent-to-treat population.

- At the extended data cutoff, the updated **HR for PFS was 0.64** (95% CI, 0.52-0.80; nominal *P*<0.0001), **favoring MIRV** over IC chemotherapy

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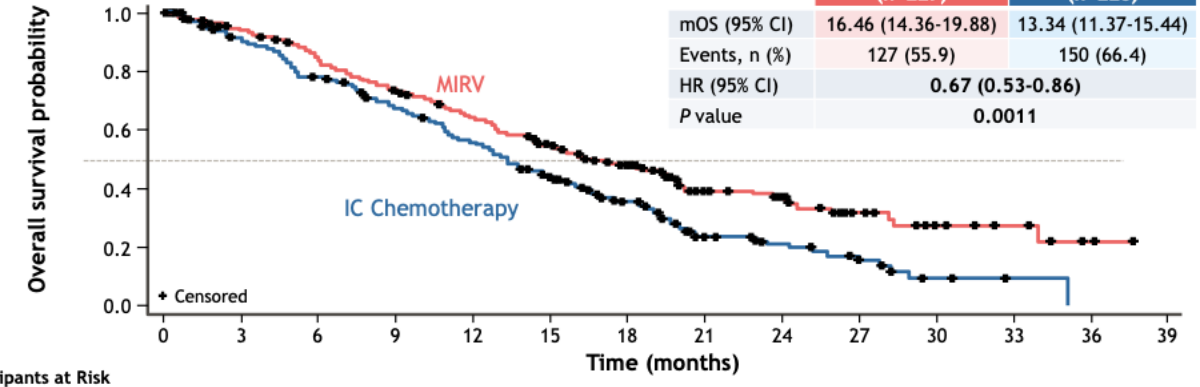
Results: Updated Overall Survival in MIRASOL

Figure 2. Post Hoc Overall Survival[a]



	MIRV (n=227)	IC Chemotherapy (n=226)
mOS (95% CI)	16.46 (14.36-19.88)	13.34 (11.37-15.44)
Events, n (%)	127 (55.9)	150 (66.4)
HR (95% CI)	0.67 (0.53-0.86)	
P value	0.0011	

No. of Participants at Risk

MIRV	227	204	178	156	134	104	74	42	30	17	9	6	2	0
IC Chemotherapy	226	185	158	133	109	79	50	23	16	10	3	1	0	

Extended data cutoff: October 27, 2023.
[a]Intent-to-treat population.

- Median follow-up time was 20.3 months (range, 19.3-21.4)
- At the extended data cutoff, the updated **HR for OS was 0.67** (95% CI, 0.53-0.86; nominal *P*=0.0011), **favoring MIRV** over IC chemotherapy

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Uterine cancer

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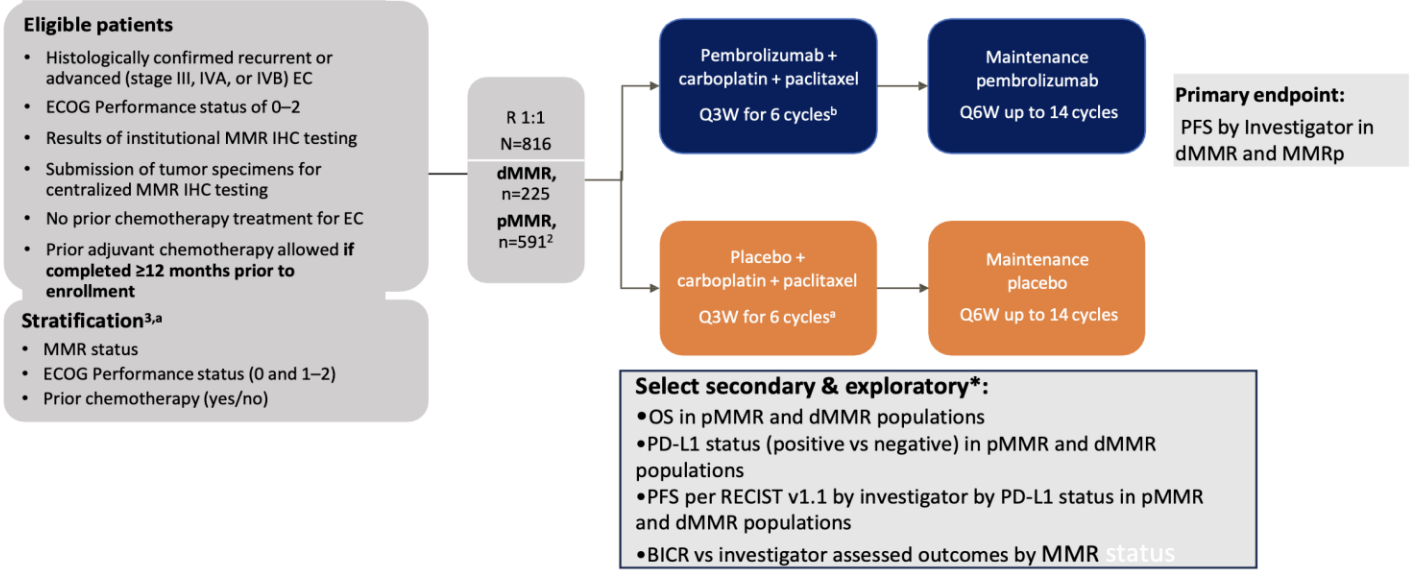
NRG-GY018: pembrolizumab plus carboplatin-paclitaxel vs placebo plus carboplatin-paclitaxel in patients with advanced/recurrent endometrial cancer



Eskander RN et al; N Engl J Med. 2023 Jun 8;388(23):2159-2170

*MMR status as randomized

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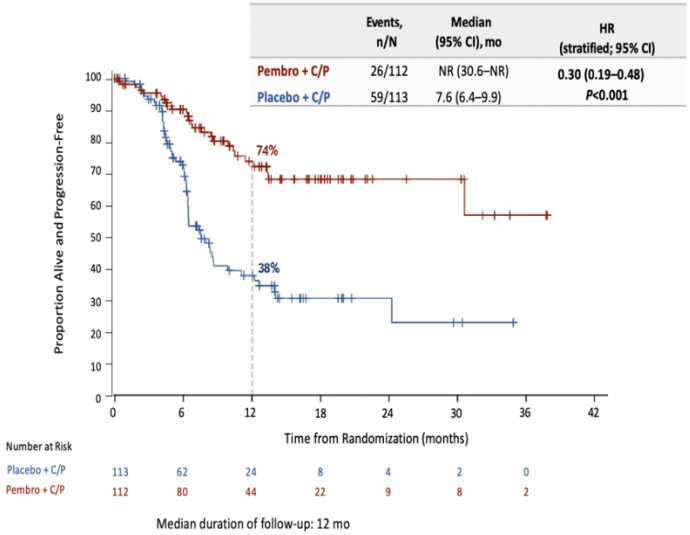
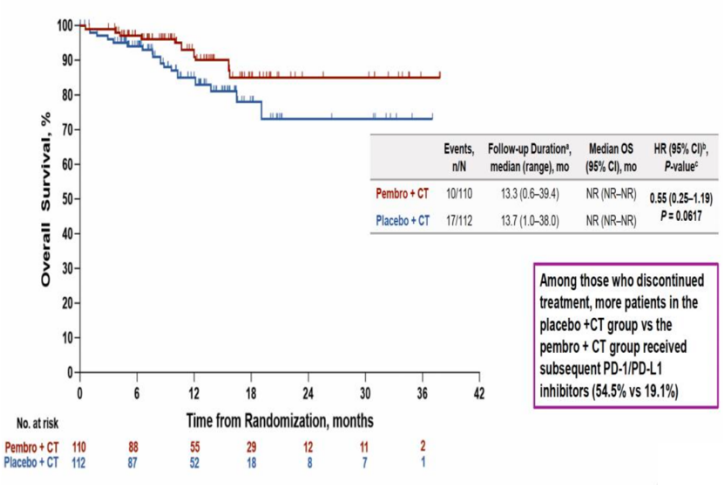
Primary End-Point:
PFS in dMMR cohort



Median duration of follow-up: 12 mo

Secondary End-Point:
OS dMMR EC*



*Immature at IA ;18% information fraction

BARCELONA 2024 ESMO congress

Eskander RN et al; N Engl J Med. 2023 Jun 8;388(23):2159-2170;

Eskander RN. et al Presented at SGO 2024 Meeting

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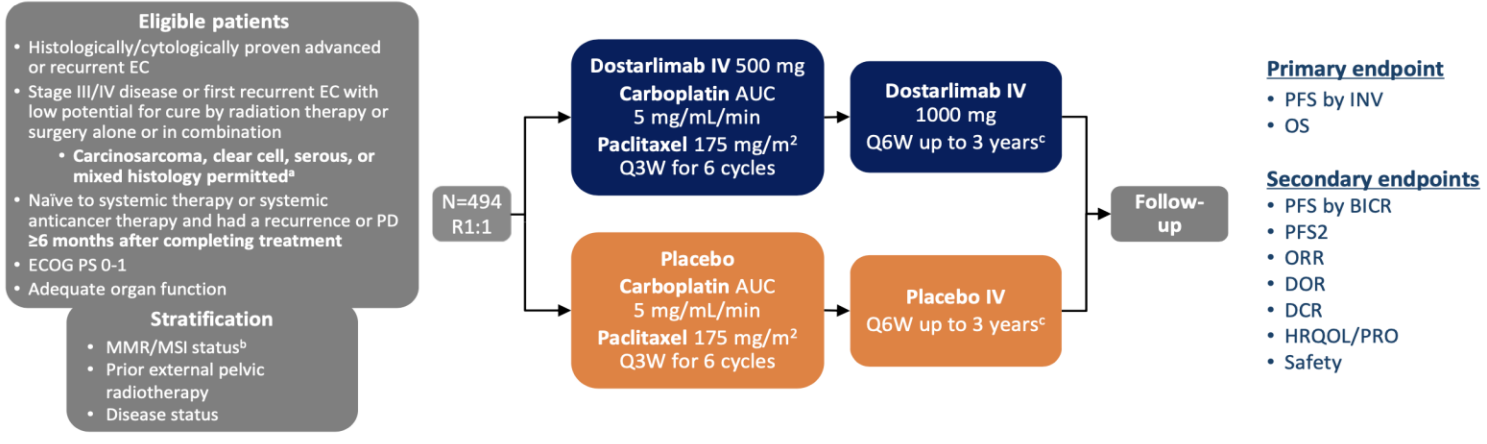
ENGOT-EN6-NSGO/GOG-3031/RUBY (NCT03981796)

Phase 3, randomized, double-blind, multicenter study of dostarlimab plus carboplatin-paclitaxel versus placebo plus carboplatin/paclitaxel in patients with primary advanced or recurrent EC



. [b]Patients were randomized based on either local or central MMR/MSI testing results. Central testing was used with local results were not available. For local determination of MMR/MSI status, IHC, next generation sequencing, and polymerase chain reaction assays were accepted. For central determination of MMR/MSI status IHC per Ventana MMR RxDx panel was used.

Mirza MR. et al N Engl J Med. 2023 Jun 8;388(23):2145-2158.

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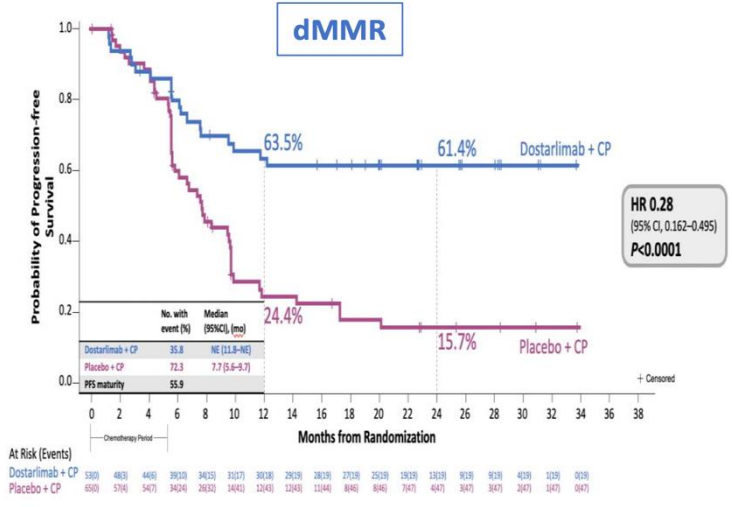
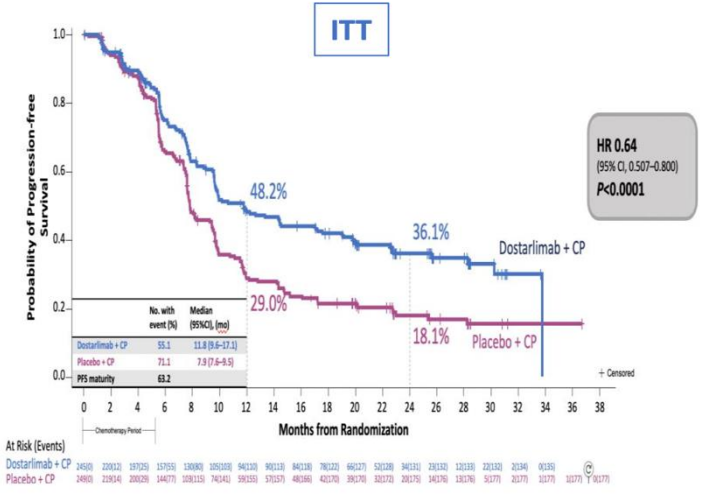
Primary End-Point: PFS in dMMR→ITT



Median duration of follow-up 24.79 months.



Median duration of follow-up 25.38 months.

Mirza MR. et al N Engl J Med. 2023 Jun 8;388(23):2145-2158.

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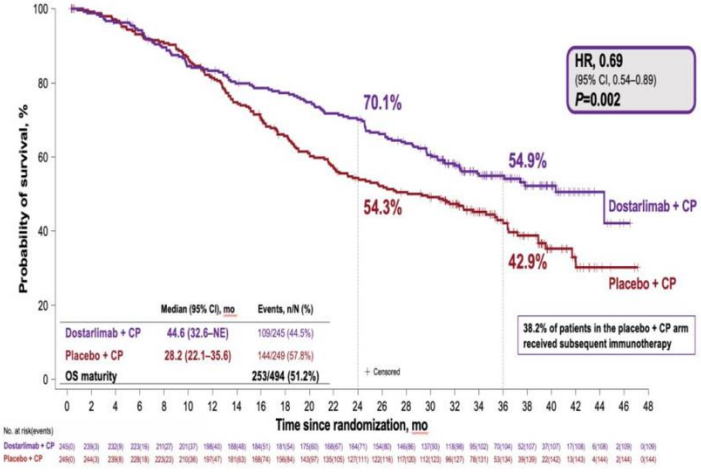
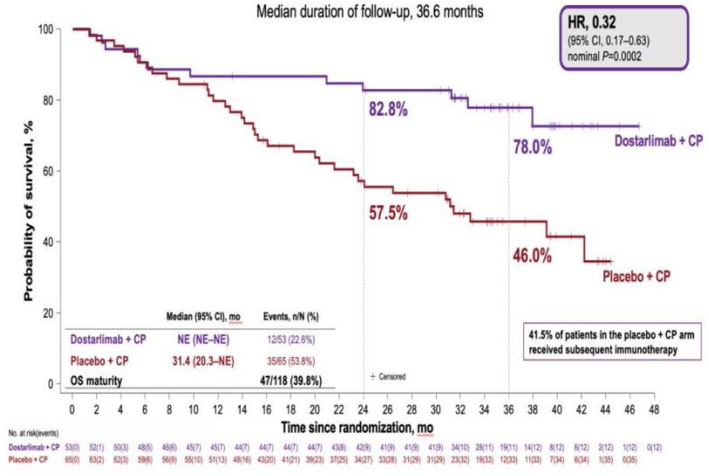
Primary End-Point: OS in ITT(IA2)

Prespecified Subgroup Analyses: OS in the dMMR/MSI-H

ITT



dMMR



BARCELONA 2024 ESMO congress

Ana Oaknin MD PhD

Matthew A. Powell et al. Presented at SGO 2024 Meeting; Matthew A. Powell et al Annals of Oncology Volume 35 - Issue 8 - 2024

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HCL HOSPICES CIVILS DE LYON | INSTITUT DE CANCÉROLOGIE

CRMT CENTRE de REFERENCE des MALADIES TROPHOBLASTIQUES

Avelumab + methotrexate to eradicate low-risk gestational trophoblastic tumors in 1st-line setting: TROPHAMET trial.

Benoit YOU [1,2,3,4] ; Jean-Pierre LOTZ [1,5] ; Pierre DESCARGUES [1,6]; Florence JOLY [4,7]; Thibault DE LA MOTTE ROUGE [4,8]; Coriolan LEBRETON [4,9] ; Laurence GLADIEFF [4,10]; Philippe FOLLANA [4,11]; Mathieu JAMELOT [1,5]; Jérome MASSARDIER [1,12]; Touria HAJRI [1]; Marine ALVES-FERREIRA [13] ; Sylvie BIN [13]; Carole LANGLOIS-JACQUES [14]; Maxime BONJOUR [14] ; Adeline ROUX [13]; Christophe DESAUW [15]; Magali PROVANSAL [16]; Vérane SCHWIERTZ [17]; Francois GOLFIER [1,2,6] ; Pierre-Adrien BOLZE [1,2,6]

1.**Centre de Référence des Maladies Trophoblastiques ; French Gestational Trophoblastic Center, Lyon, France**; 2.Univ Lyon ; Université Claude Bernard Lyon; 2 Faculté de médecine Lyon-Sud ; EA 3738 CICLY ; Lyon ; France ; 3.Medical Oncology ; Institut de Cancérologie des Hospices Civils de Lyon (IC-HCL) ; CITOHL ; EPSILYON; Hospices Civils de Lyon, Lyon, France; 4.GINECO, Paris, France; 5.Hôpital Tenon, Pôle Onco-Hématologie Hôpitaux Universitaires de l'Est Parisien, APHP, Université Pierre et Marie Curie, Paris, France; 6.Service de Chirurgie Gynécologique et Oncologique, Obstétrique, Centre Hospitalier Lyon Sud, Hospices Civils de Lyon ; Pierre Bénite, France; 7.Clinical Research Department, Centre François Baclesse, 3 avenue du Général Harris, F-14076 Caen cedex 05, France; 8.Centre Eugene Marquis, Rennes, France; 9.Institut Bergonié, Bordeaux, France; 10.Département d'oncologie médicale ; Institut Claudius Regaud ; IUCT-ONCOPOLE ; Toulouse ; France; 11.Centre Antoine Lacassagne, Nice, France; 12.Service de Gynécologie Obstétrique, Unité de Diagnostic Anténatal, Hôpital Femme Mère Enfant, Hospices Civils de Lyon ; Bron, France; 13.Service Recherche et Epidémiologie Cliniques - Pôle de Santé Publique , Hospices Civils de Lyon, Lyon, France; 14.Biostatistiques - Pôle de Santé Publique , Hospices Civils de Lyon, Lyon, France; 15.CHU Lille – Hôpital HURIEZ, Lille, France; 16.Institut Paoli-Calmettes, Marseille, France; 17. URCC, HCL; Lyon, France

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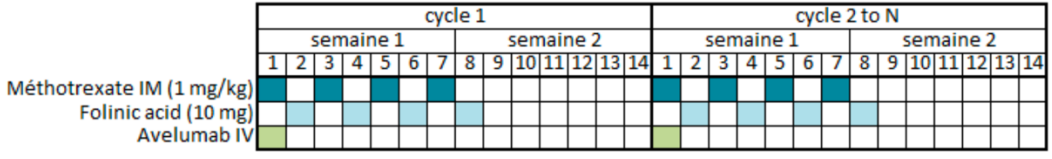
TROPHAMET trial design (NCT04396223)

Study Treatment

- **Treatment**
  - **8-day MTX regimen:** Methotrexate 1 mg/kg IM on days 1, 3, 5, 7 alternating with oral Folinic acid; Q2weeks
  - **Avelumab**: Flat dose with IV 800 mg every 2 weeks, on days 1 before MTX



- **Administration until hCG normalization**, followed by **3 consolidations cycles**

TROPHAMET trial outcomes (NCT04396223)

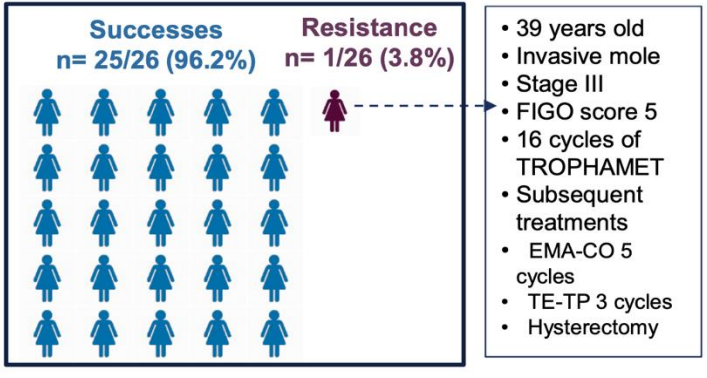
Efficacy: Primary Endpoint

- Number of Avelumab cycles: median, 8 (range: 2-21)
- Number of MTX cycles median, 8 (range: 3-21)

- **Successful hCG normalization rate:**

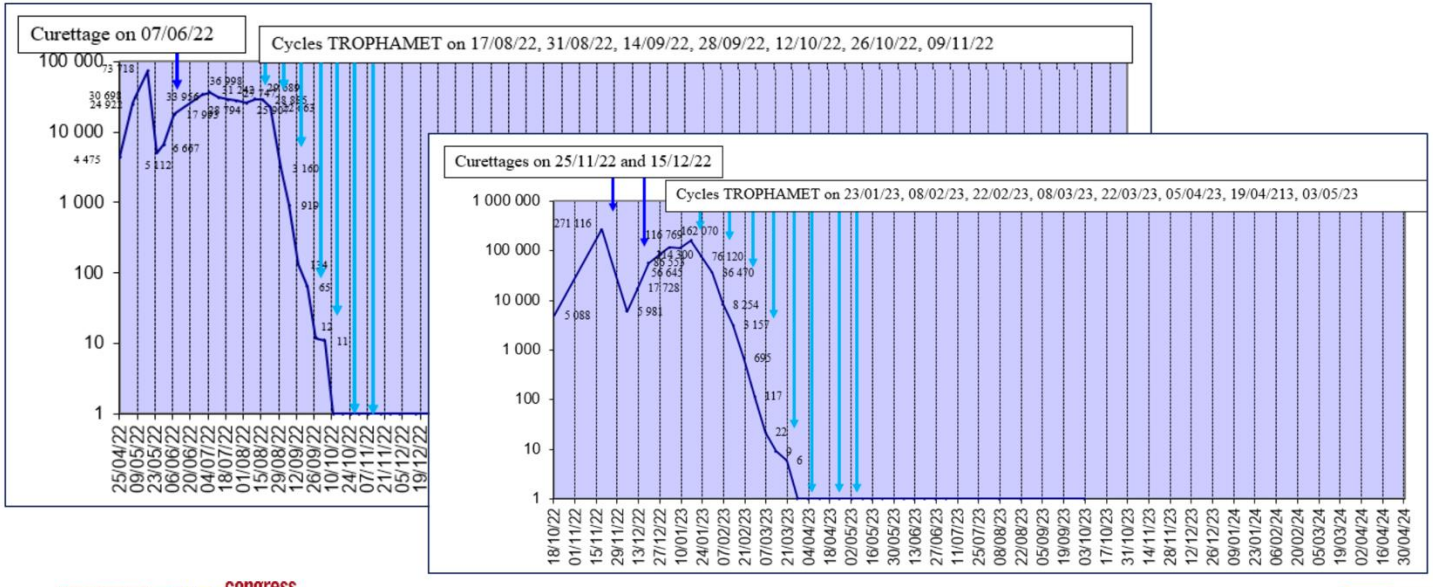
⇒ **96.2% patients (95% CI [85.8-97.3]; n=25/26)**

- Time to hCG normalization: median, 3.32 months (IQR 2.51-4.02)



TROPHAMET trial outcomes (NCT04396223)

Efficacy: Examples of Fast hCG Declines



Cervical (vaginal & vulvar) cancers

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A randomised phase III trial of induction chemotherapy followed by chemoradiation compared with chemoradiation alone in locally advanced cervical cancer.

The GCIG INTERLACE trial

M. McCormack[1], D. Gallardo[2], G. Eminowicz[1], P. Diez[3], L. Farrelly[4], C. Kent[5], E. Hudson[6], M. Panades[7], T. Mathew[8], A. Anand[9], M. Persic[10], J. Forrest[11], R. Bhana[12], N. Reed[13], A. Drake[14], H. Stobart[15], A. Mukhopadhyay[16], A.M. Hacker[4], A. Hackshaw[4], J.A. Ledermann[4]

[1]University College Hospital NHS Trust, London, UK; [2]INCAN, Mexico; [3]East and North Hertfordshire NHS trust, UK; [4]University College London CTC, UK; [5]University of Leicester NHS trust, UK; [6]Velindre Cancer Centre, UK; [7]United Lincolnshire Hospitals NHS Trust, UK; [8]Sheffield Teaching Hospitals NHS Trust, UK; [9]Nottingham University NHS Trust, UK; [10]University of Derby and Burton NHS Foundation Trust, UK; [11]Royal Devon and Exeter NHS Foundation Trust, UK; [12]University Hospital of North Midlands NHS Trust, UK; [13]Beatson West of Scotland Cancer Centre, UK; [14]Belfast Health and Social Care Trust, UK; [15]Independent Cancer Patients' Voice, UK; [16]Kolkata Gynaecological Oncology Trials and Translational Research Group, Kolkata India

CRUK grant number: C37815/A12832

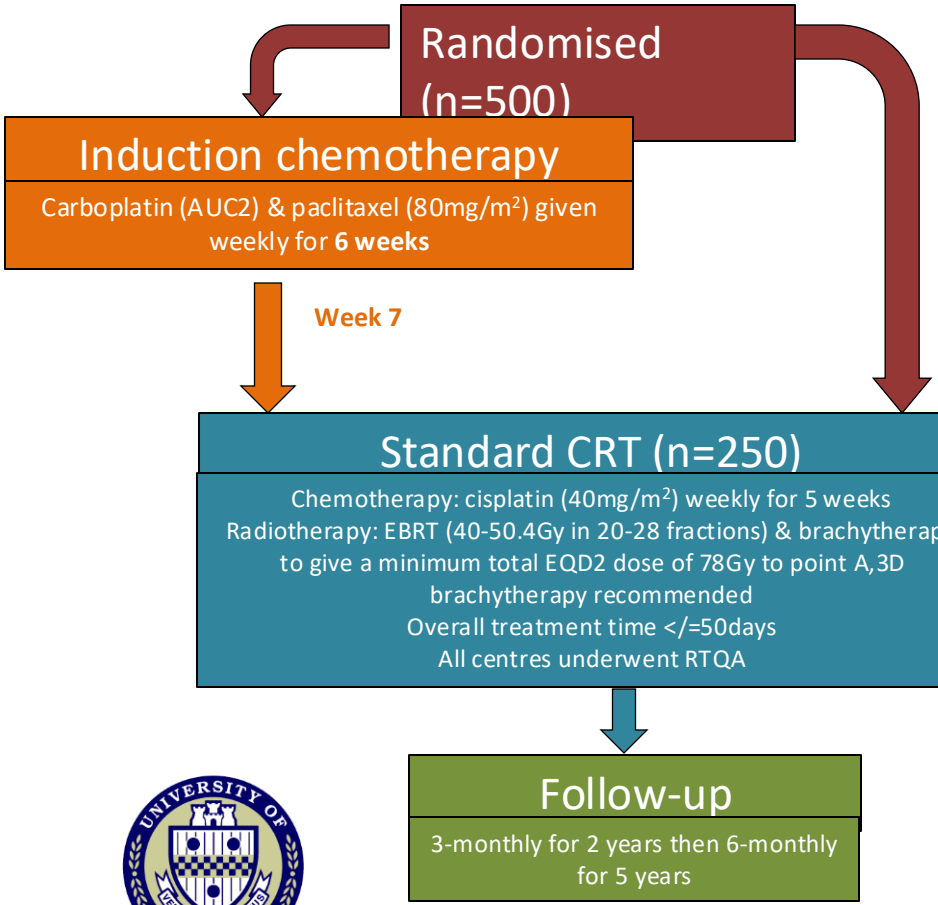
University of Pittsburgh

INTERLACE Trial Design

Key eligibility criteria

- Newly diagnosed histologically confirmed FIGO (2008) stage IB1 node+,IB2 ,II,IIIB,IVa squamous, adeno, adenosquamous cervical cancer
- No nodes above aortic bifurcation
- Adequate renal/liver and bone marrow function
- Fit for chemotherapy & radical RT
- No prior pelvic RT

RT=Radiation
IMRT=Intensity modulated radiation
EBRT=External beam radiation
BT= Brachytherapy
RTQA=Radiation quality assurance



Stratified by

- Site
- Stage
- Nodal status
- 3D v IMRT EBRT
- 2D v 3D BT
- Tumour size
- SCC v other

Primary endpoints

- PFS
- OS

Secondary endpoints

- Adverse events
- Pattern of relapse
- QOL
- Time to subsequent treatment

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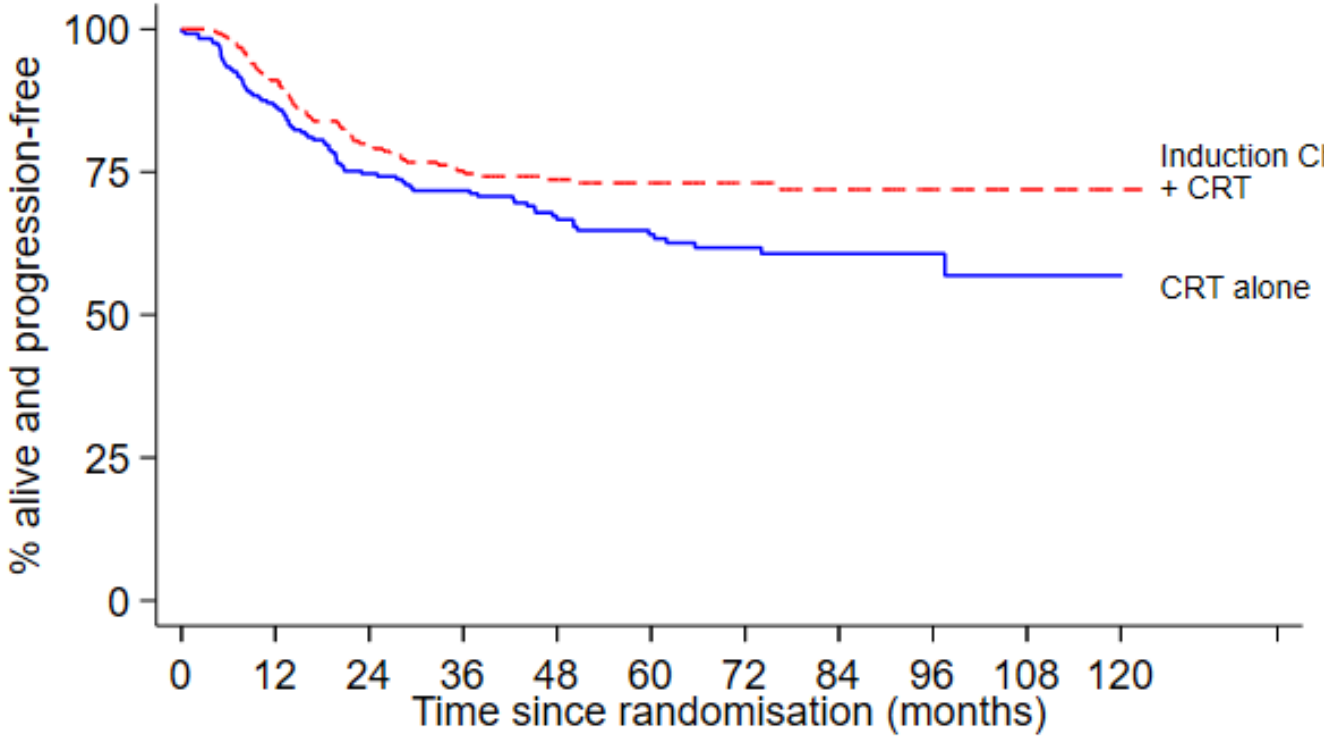
INTERLACE Progression-Free Survival (median FU 64m)

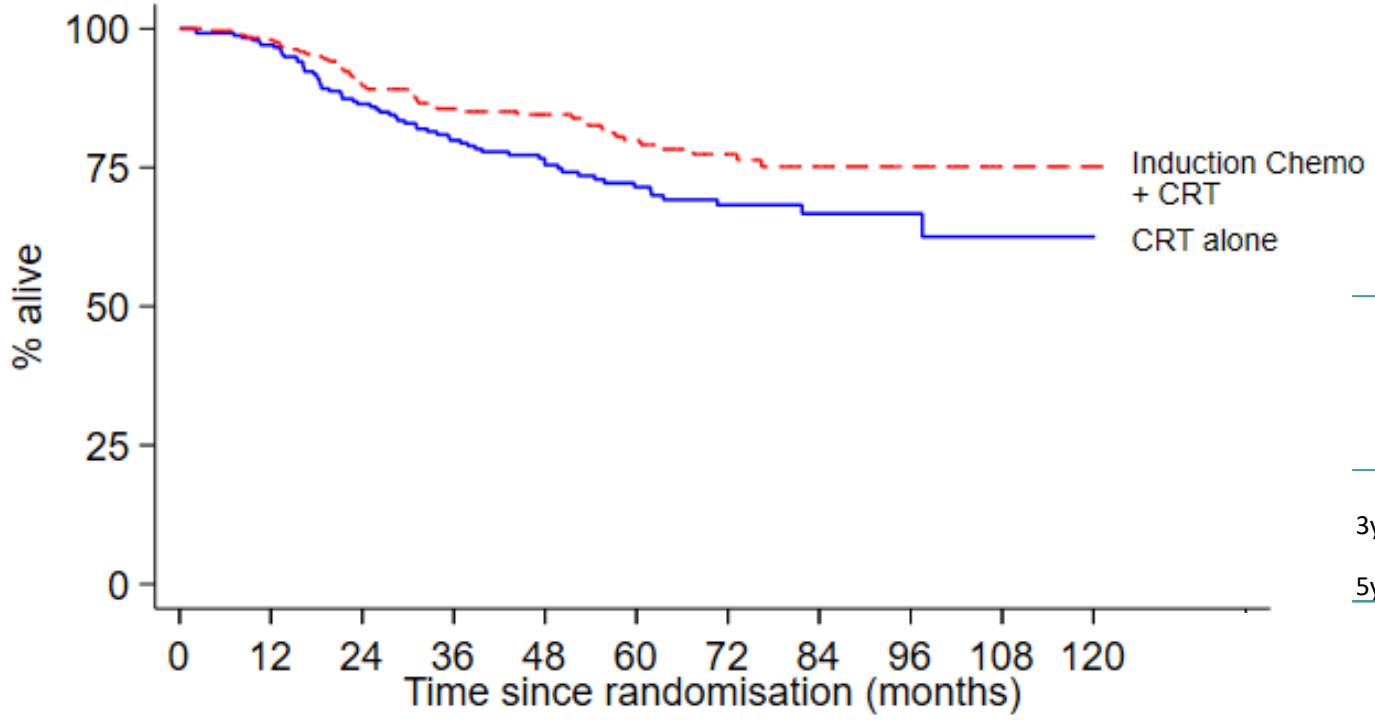


146 PFS events
HR 0.65;95% CI:0.46 -0.91
P=0.013

	Induction Chemo+ CRT (n=250)	CRT alone (n=250)
3yr PFS	75%	72%
5yr PFS	73%	64%

Number at risk											
CRT alone	250	204	157	140	110	88	63	36	16	5	1
Induction Chemo + CRT	250	220	178	152	132	105	72	40	19	8	1

INTERLACE Overall Survival (median FU 64m)



109 deaths
HR 0.61;95% CI: 0.40-0.91
P=0.04

	Induction Chemo + CRT (n=250)	CRT alone (n=250)
3yr OS	86%	80%
5yr OS	80%	72%

Number at risk

CRT alone	250	228	181	154	124	99	67	39	16	5	1
Induction Chemo + CRT	250	236	195	168	146	111	75	42	19	8	1

GCIG GYNECOLOGIC CANCER INTERGROUP
CANCER RESEARCH UK
CANCER TRIALS CENTRE

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Pembrolizumab Plus Chemoradiotherapy for High-Risk Locally Advanced Cervical Cancer: The Randomized, Double-Blind, Phase 3 ENGOT-cx11/GOG-3047/KEYNOTE-A18 Study

Domenica Lorusso,[1] Yang Xiang,[2] Kosei Hasegawa,[3] Giovanni Scambia,[4] Manuel Leiva,[5] Pier Ramos-Elias,[6] Alejandro Acevedo,[7] Julia Vizkeleti,[8] Andrea Gomes,[9] Fernando Contreras Mejía,[10] Ari Reiss,[11] Ali Ayhan,[12] Jung-Yun Lee,[13] Valeriya Saevets,[14] Flora Zagouri,[15] Kan Li,[16] Karin Yamada,[16] Sarper Toker,[16] Sandro Pignata,[17*] Linda R. Duska[18*] on behalf of the ENGOT-cx11/GOG-3047/KEYNOTE-A18 investigators

[1]Gynaecology Oncology Unit, Fondazione Policlinico Universitario A Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy; [2]Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, National Clinical Research Center for Obstetric & Gynecologic Diseases, Beijing, China; [3]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [4]Scientific Directorate, Fondazione Policlinico Universitario Agostino Gemelli IRCCS and Catholic University of the Sacred Heart, Rome, Italy; [5]Instituto de Oncologia y Radioterapia Clinica Ricardo Palma, Lima, Peru; [6]Integra Cancer Institute, Edificio Integra Medical Center, Guatemala City, Guatemala; [7]Oncocentro, Valparaiso, Chile; [8]National Institute of Oncology, Centre of Radiotherapy, Budapest, Hungary; [9]Liga Norte Riograndense Contra o Cancer Rio Grande do Norte, Brazil; [10]Instituto Nacional de Cancerologia, Bogota, Colombia; [11]Rambam Medical Center, Gyneco-oncology Unit, Haifa, Israel; [12]Turkish Society of Gynecologic Oncology (TRSGO), Başkent University, Ankara, Turkiye; [13]Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; [14]Chelyabinsk Regional Clinical Center Oncology and Nuclear Medicine, Chelyabinsk, Russia; [15]Alexandra Hospital, Athens, Greece; [16]Merck & Co., Inc., Rahway, NJ, USA; [17]Department of Urology and Gynecology, Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli, Italy; [18]University of Virginia School of Medicine, Charlottesville, VA, USA

*Drs. Pignata and Duska contributed equally to this presentation.

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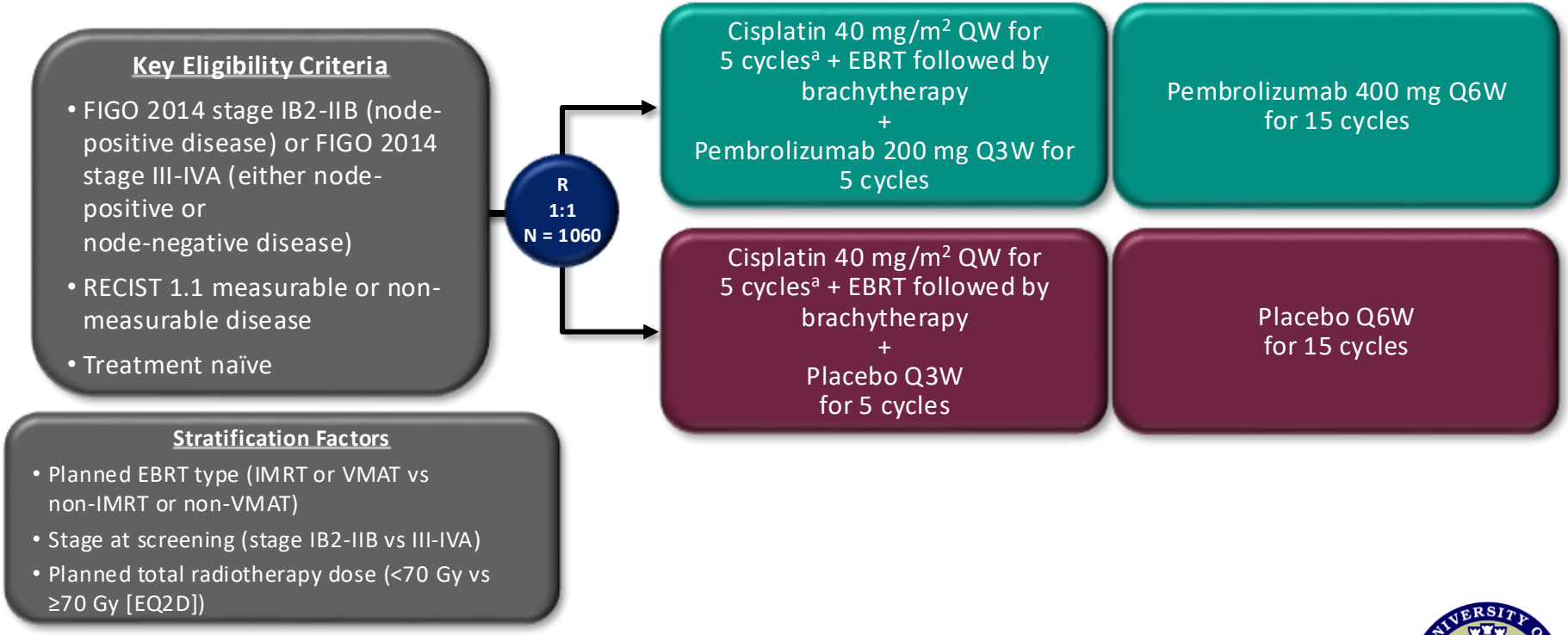
ENGOT-cx11/GOG-3047/KEYNOTE-A18: Randomized, Double-Blind, Phase 3 Study



[a]A 6th cycle was allowed per investigator discretion. EBRT, external beam radiotherapy; FIGO, International Federation of Gynecology and Obstetrics; Gy, grays; IMRT, intensity-modulated radiotherapy; Q3W, every 3 weeks; Q6W, e… RECIST, Response Evaluation Criteria in Solid Tumors; VMAT, volumetric-modulated arc therapy. ENGOT-cx11/GOG-3047/KEYNOTE-A18 ClinicalTrials.gov identifier, NCT04221945.

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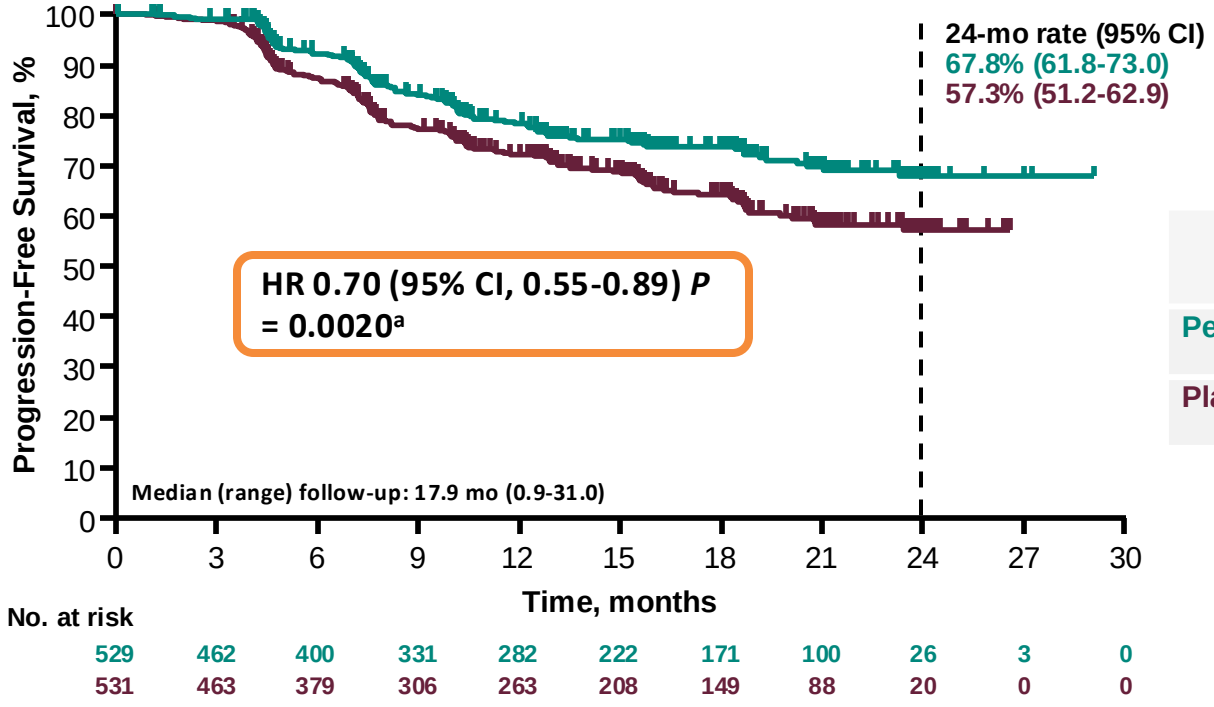
Primary Endpoint: Progression-Free Survival



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	21.7%	NR (NR-NR)
Placebo Arm	29.0%	NR (NR-NR)

Response assessed per RECIST v1.1 by investigator review or histopathologic confirmation. [a]With 269 events (88.5% information fraction), the observed $P = 0.0020$ (1-sided) crossed the prespecified nominal boundary of 0.0172 (1-sided) for first interim analysis. The success criterion of the PFS hypothesis was met, and thus no formal testing of PFS will be performed at a later analysis. Data cutoff date: January 9, 2023.

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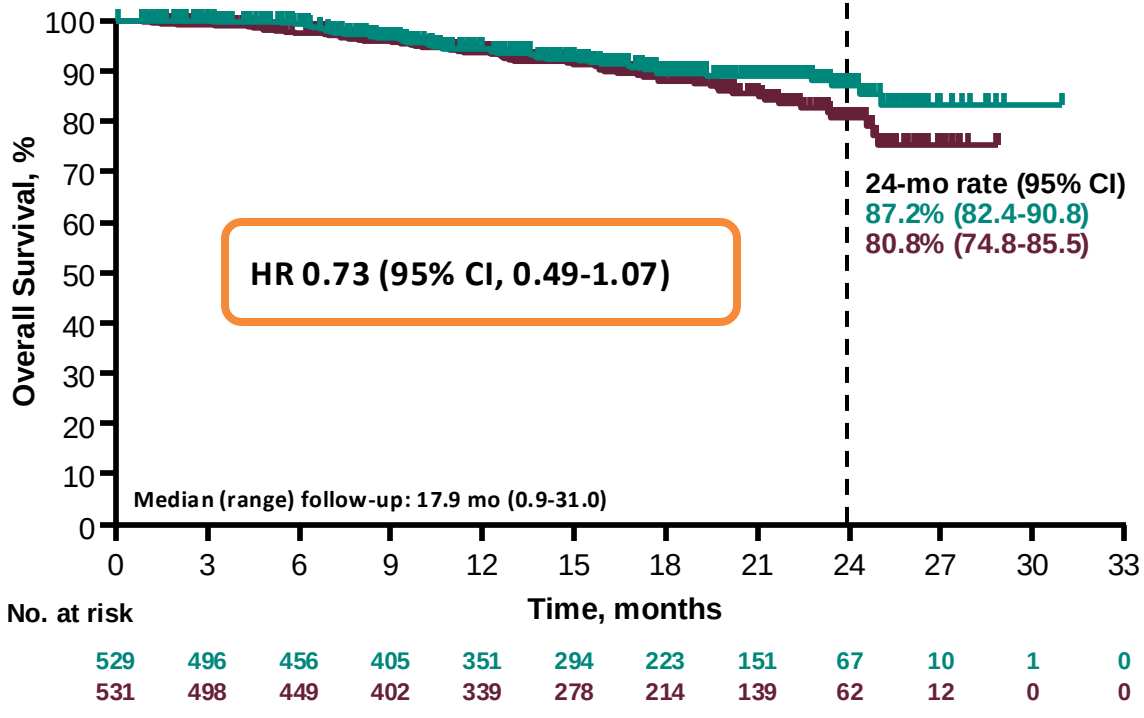
Primary Endpoint: Overall Survival



	Pts w/ Event*	Median, mo (95% CI)
Pembro Arm	8.3%	NR (NR-NR)
Placebo Arm	11.1%	NR (NR-NR)

*42.9% information fraction[a]

[a]At this analysis, 103 of the 240 deaths expected at the final analysis had occurred.
Data cutoff date: January 9, 2023.

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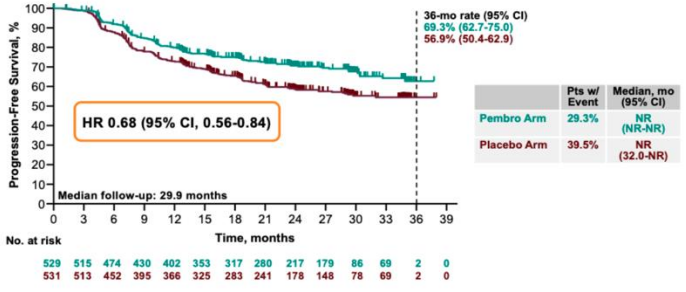
ENGOT-cx11/GOG-3047/KEYNOTE-A18

Strengths

Updated Progression-Free Survival at IA2

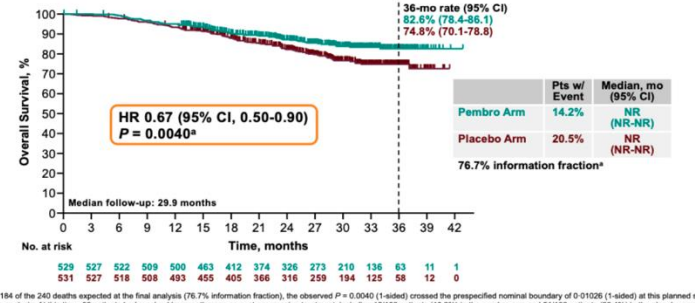


	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	29.3%	NR (NR-NR)
Placebo Arm	39.5%	NR (32.0-NR)

Response assessed per RECIST v1.1 by investigator review or histopathologic confirmation. Since the success criterion of the PFS hypothesis was met at IA1, no formal testing of PFS was performed at IA2.
Data cutoff date: January 8, 2024.

Domenica Lorusso

Primary Endpoint: Overall Survival at IA2



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	14.2%	NR (NR-NR)
Placebo Arm	20.5%	NR (NR-NR)

76.7% information fraction[a]

[a]With 184 of the 240 deaths expected at the final analysis (76.7% information fraction), the observed $P = 0.0040$ (1-sided) crossed the prespecified nominal boundary of 0.01026 (1-sided) at this planned second interim analysis. At this time, 66 patients had received immunotherapy as post-progression treatment, including 15/138 patients (10.9%) in the pembro arm and 51/193 patients (26.4%) in the placebo arm; of those, 10 (7.2%) and 41 (21.2%), respectively, had received pembro. Data cutoff date: January 8, 2024.

Domenica Lorusso

- Median follow-up: 29.9 months; majority disease events expected in first 2-years
- **At 3-years: 12% PFS benefit (HR 0.68) and 8% OS benefit (HR 0.67)**
- Treatment related adverse events grade≥3 69.1% vs 61.3%, difference mainly due to immune-mediated AE's.
- Patient reported HRQoL (global health status, physical functioning) changes similar to placebo arm

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innovaTV 301/ENGOT-cx12/GOG-3057: A Global, Randomized, Open-Label, Phase 3 Study of Tisotumab Vedotin vs Investigator's Choice of Chemotherapy in 2L or 3L Recurrent or Metastatic Cervical Cancer

Prof. Em. Dr. Ignace Vergote

University Hospitals Leuven, Katholieke Universiteit Leuven, Leuven, and Belgium and Luxembourg Gynaecological Oncology Group, Belgium, European Union

Antonio González Martín, Keiichi Fujiwara, Elsa Kalbacher, Andrea Bagaméri, Sharad Ghamande, Jung-Yun Lee, Susana Banerjee, Fernando Maluf, Domenica Lorusso, Kan Yonemori, Els Van Nieuwenhuysen, Luis Manso Sanchez, Linn Woelber, Anneke Westermann, Allan Covens, Elizabeth Whalley, Melinda Siew Leng Teng, Ibrahima Soumaoro, Brian M. Slomovitz

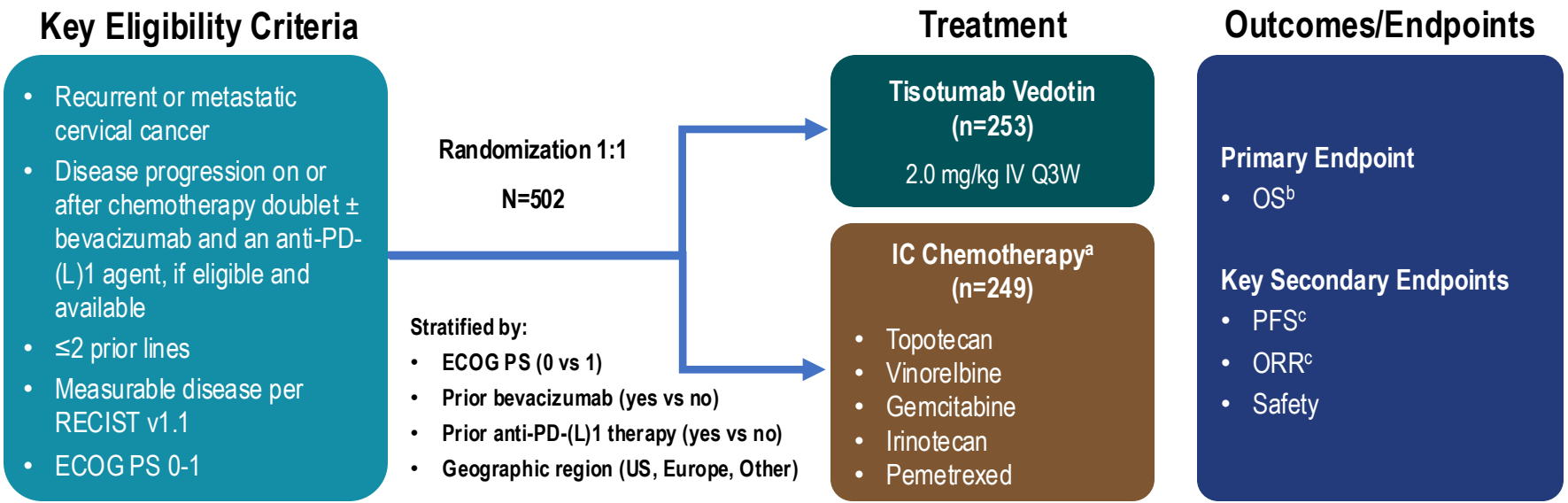
ENGOT European Network of Gynaecological Oncological Trial groups

BGOG Belgian Gynaecological Oncology Group

GOG FOUNDATION® Transforming the standard of care

University of Pittsburgh

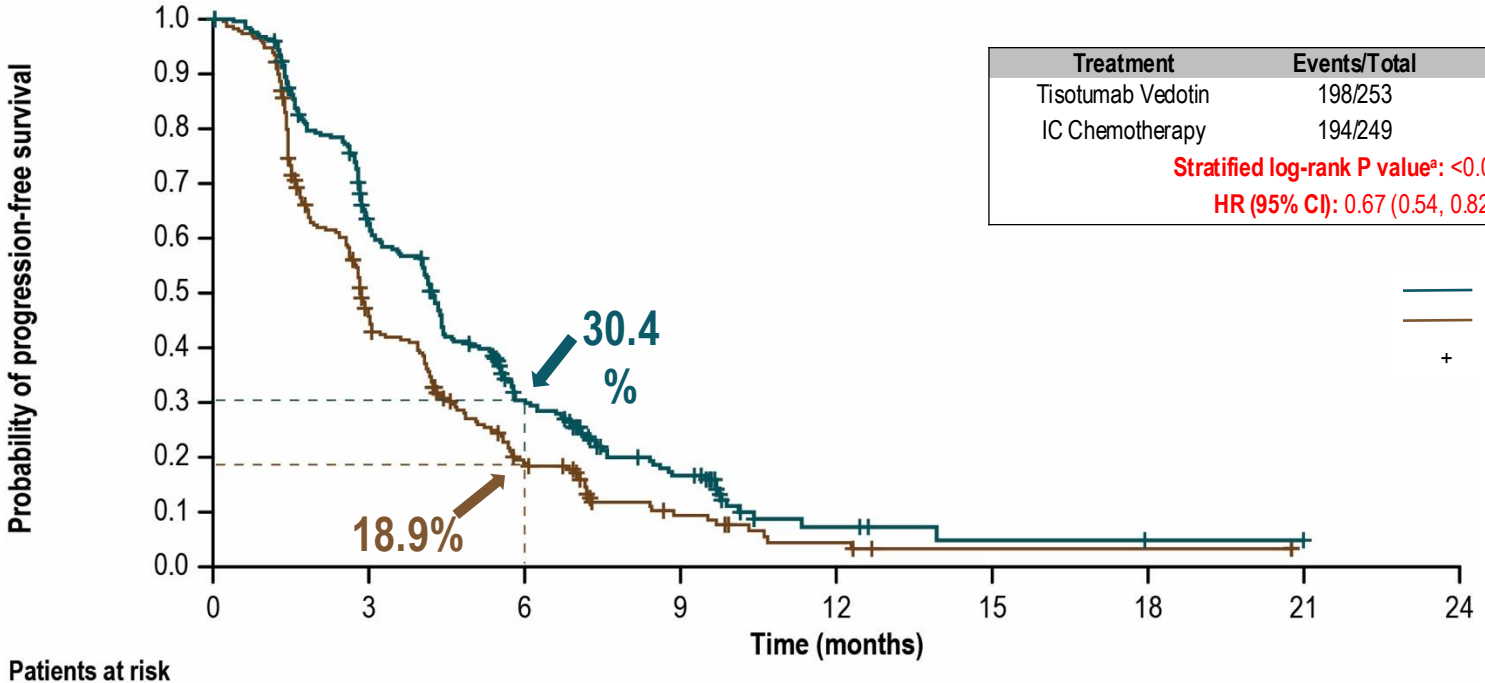
innovaTV 301: A Randomized, Open-Label, Phase 3 Trial



- Data presented herein are a planned interim analysis

IC, investigator's choice
End of treatment visit occurred 30 days after the last dose of treatment. Survival follow-up occurred every 60 days after the last dose of treatment.
[a]Chemotherapy regimens were given at the following doses: topotecan: 1 or 1.25 mg/m^2 IV on Days 1 to 5, every 21 days; vinorelbine: 30 mg/m^2 IV on Days 1 and 8, every 21 days; gemcitabine: 1000 mg/m^2 IV on Days 1 and 8, every 21 days; irinotecan: 100 or 125 mg/m^2 IV weekly for 28 days, every 42 days; pemetrexed: 500 mg/m^2 on Day 1, every 21 days; [b]OS was defined as the time from the date of randomization to the date of death due to any cause; [c]Assessed by investigator.

Progression-Free Survival Per Investigator



Treatment	Events/Total	Median (95% CI)
Tisotumab Vedotin	198/253	4.2 (4.0, 4.4)
IC Chemotherapy	194/249	2.9 (2.6, 3.1)

Stratified log-rank P value[a]: <0.0001

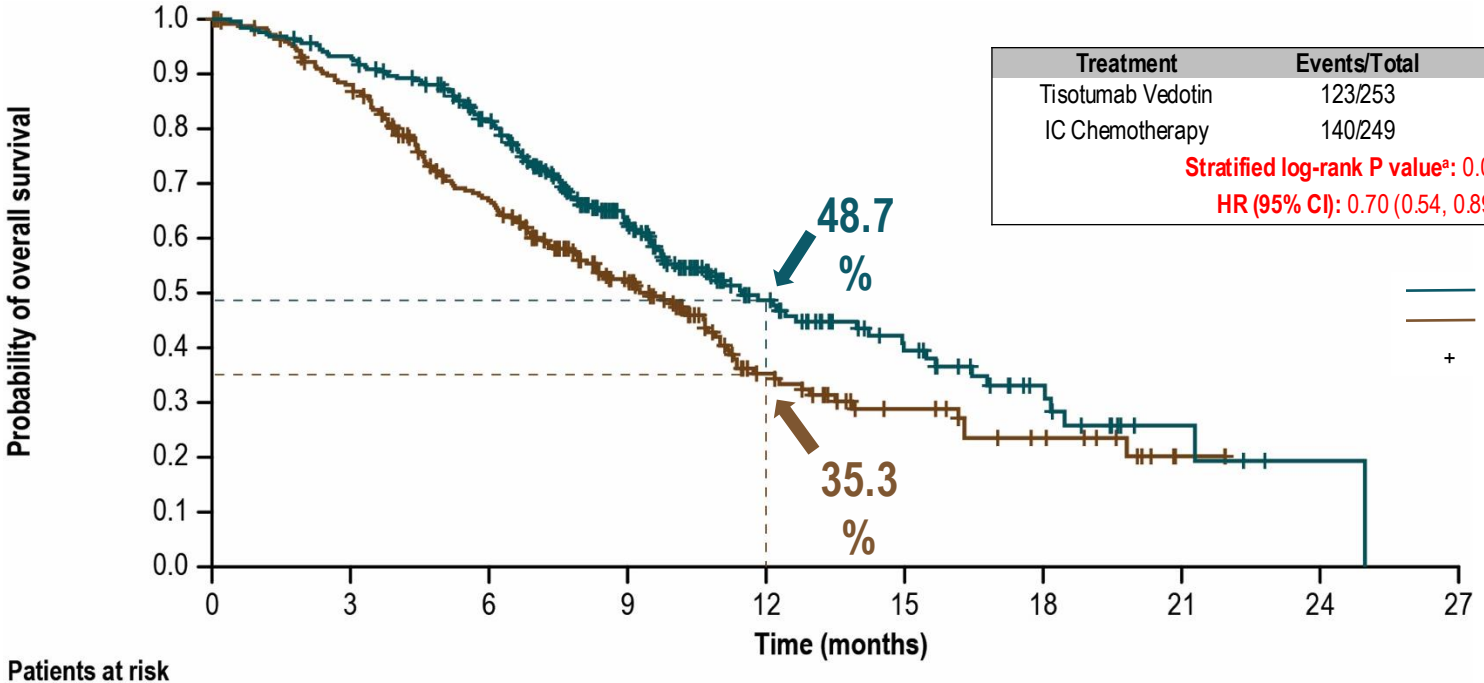
HR (95% CI): 0.67 (0.54, 0.82)

Patients at risk

Tisotumab vedotin	253	148	62	25	5	2	1	0	0
IC Chemotherapy	249	96	34	11	4	1	1	0	0

[a]The threshold for statistical significance is 0.0453 (2-sided), based on the actual number of PFS events at interim analysis.

Overall Survival (Primary Endpoint)



Treatment	Events/Total	Median (95% CI)
Tisotumab Vedotin	123/253	11.5 (9.8, 14.9)
IC Chemotherapy	140/249	9.5 (7.9, 10.7)

Stratified log-rank P value[a]: 0.0038

HR (95% CI): 0.70 (0.54, 0.89)

Patients at risk

Tisotumab vedotin	253	234	191	109	52	29	14	4	1	0
IC Chemotherapy	249	212	150	87	37	19	11	1	0	0

[a]The threshold for statistical significance is 0.0226 (2-sided), based on the actual number of OS events at interim analysis.

Thank you

UPMC Magee-Women's Hospital

Pittsburgh

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