AGGIORNAMENTO ASCO

Roberta Massobrio, Silvia Ficarelli

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Ovarian cancer

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2023 ASCO ANNUAL MEETING

Hyperthermic intraperitoneal chemotherapy in ovarian cancer

Final survival analysis of the phase III OVHIPEC-1 trial

S.L. Aronson, M.I. Lopez-Yurda, S.N. Koole, J.H. Schagen van Leeuwen, H.W. Schreuder, R.H. Hermans, I.H. de Hingh, M.D. van Gent, H.J. Arts, M.A. van Ham, P.A. van Dam, P. Vuylsteke, A.G. Aalbers, V.J. Verwaal, K.K. Van de Vijver, N.K. Aaronson, **G.S. Sonke***, W.J. van Driel*

*shared last author

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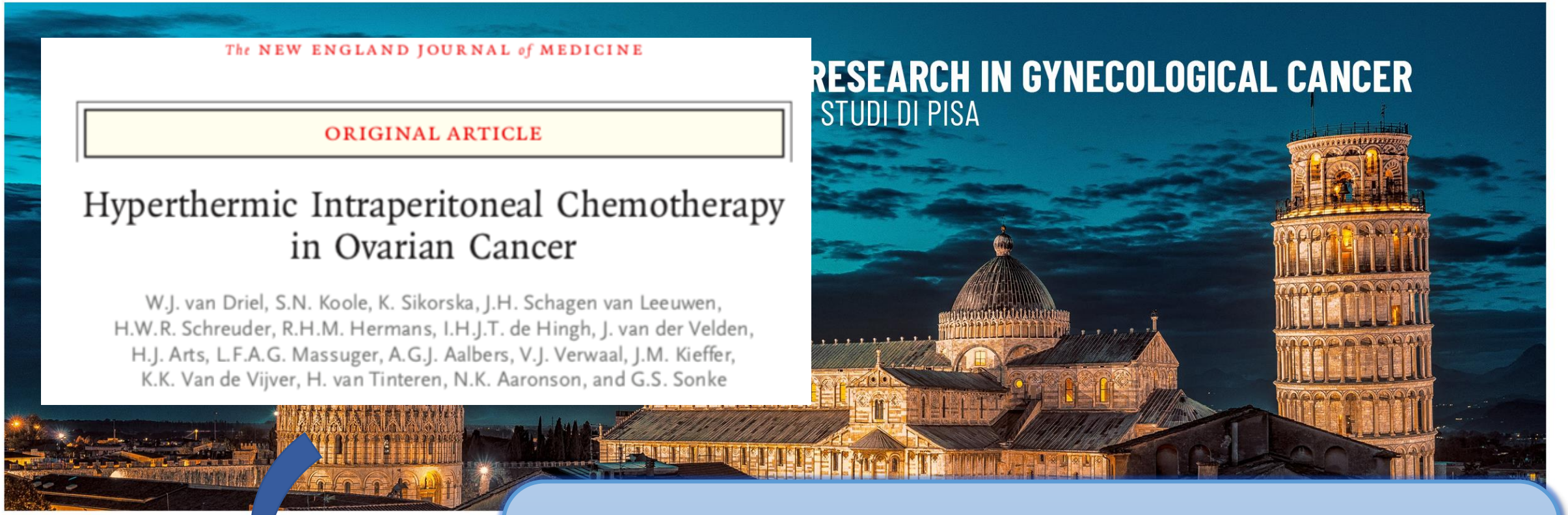

- **First RCT to evaluate HIPEC in ovarian cancer**
- **Improved recurrence-free survival and overal survival at 4.7 years of follow up**
- **No increase of adverse events or delayed start of adjuvant chemotherapy**

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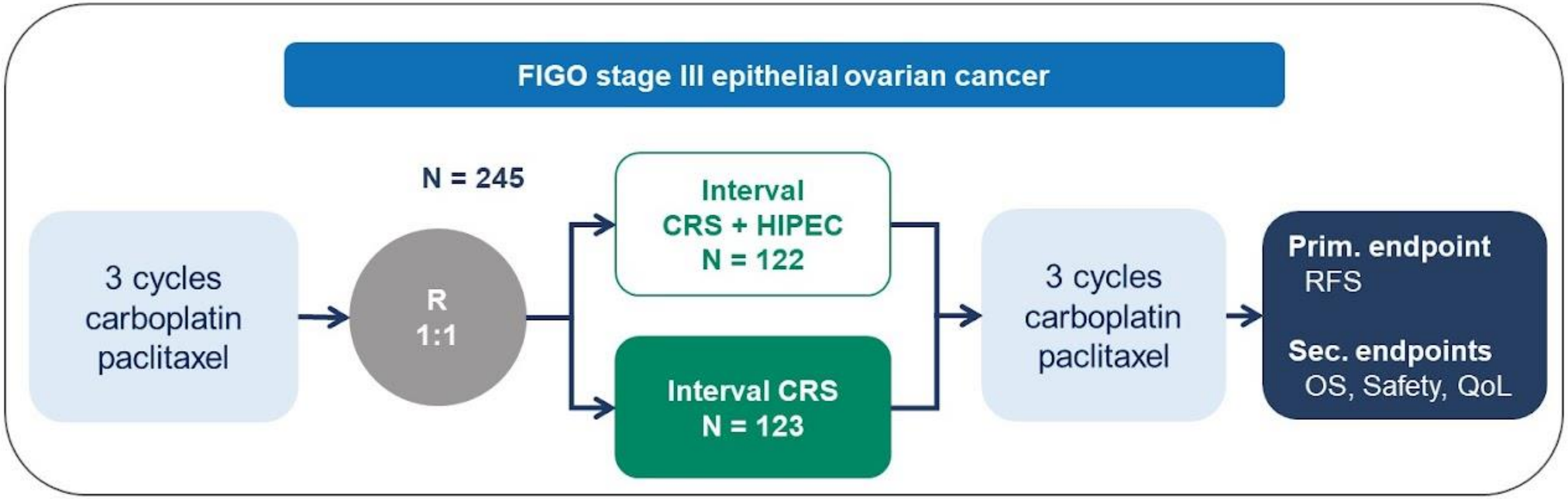
Study design



- Accrual between 2007-2016 in 8 centers in the Netherlands and Belgium
- Patients required neo-adjuvant chemotherapy due to extensive disease
- Follow-up visits every 3 months in year 1-2, every 6 months thereafter

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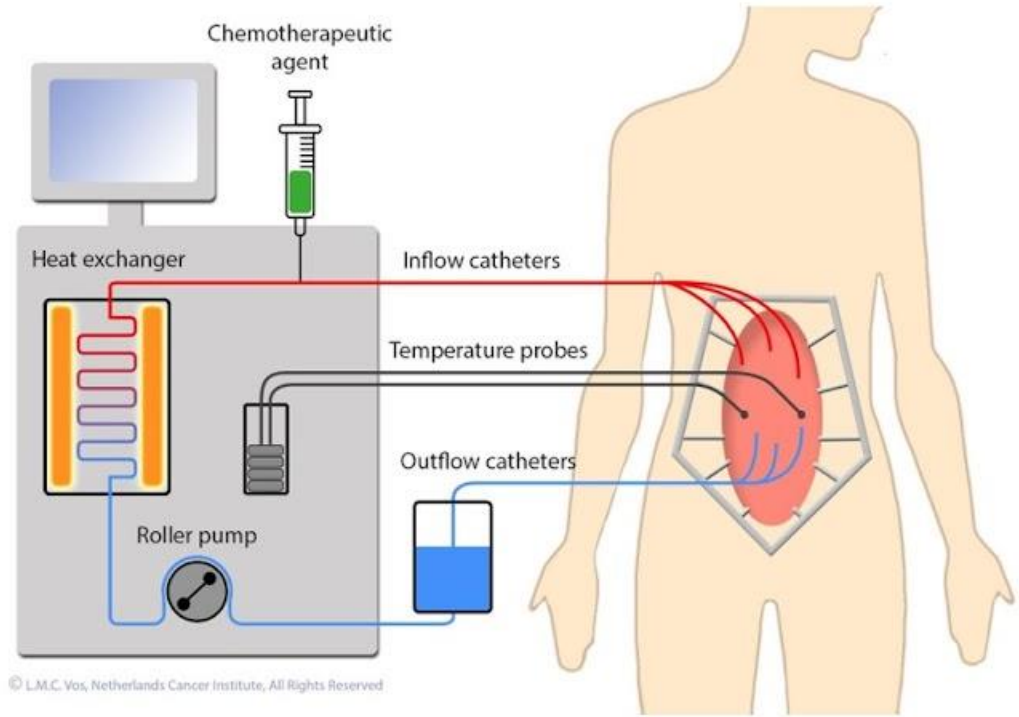
HIPEC procedure

- Open ‘colosseum’ technique
- Cisplatin 100 mg/m²
  - 50% at the start
  - 25% after 30 min
  - 25% after 60 min
- Heated to 42°C, min flow of 1L/min
- Sodium thiosulfate for renal protection



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Treatment characteristics

	CRS-HIPEC (N=122)	CRS (N=123)
Residual disease after surgery – no. (%)		
R-1, no visible tumor, complete CRS	84 (69)	82 (67)
R-2, residual tumor 2.5 - 10mm	35 (29)	38 (31)
Incomplete CRS >10mm	3 (2)	3 (2)
Bowel resections – no. (%)		
No bowel resection performed	92 (75)	92 (75)
Bowel resection with ileo- or colostomy	21 (17)	13 (11)
Bowel resection without ileo- or colostomy	8 (7)	17 (14)
Median duration of surgery (including HIPEC) – min (IQR)	338 (299–426)	190 (150–250)
Median duration of hospitalization – days (IQR)	10 (8–12)	8 (7–10)
Median time between surgery and start adjuvant chemotherapy – days (IQR)	33 (28–41)	30 (25–41)

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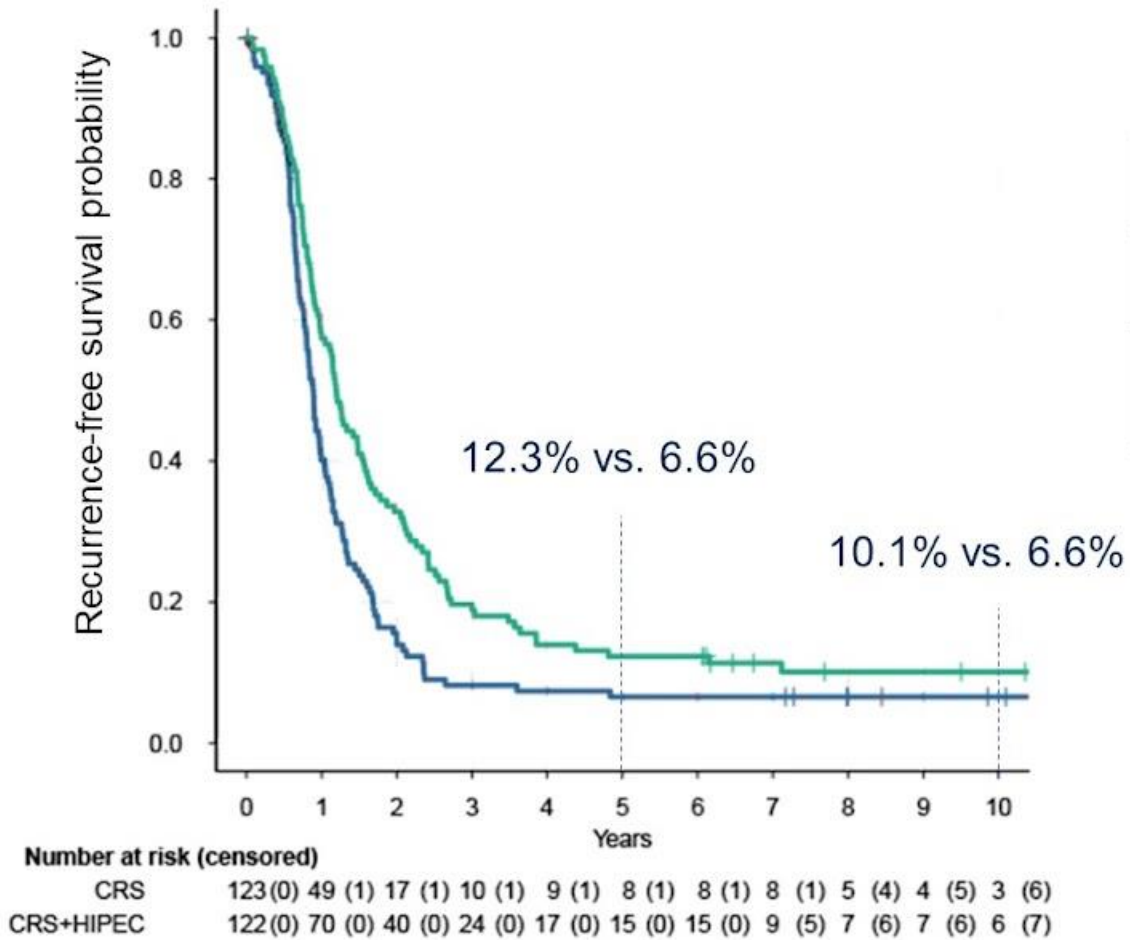
RFS after ten years of follow-up



	CRS-HIPEC	CRS
Median RFS, mo	14.3	10.7
HR (95%CI)	**0.63 (0.48 – 0.83)**	
Stratified log-rank p	0.0008	

HIPEC delays recurrence

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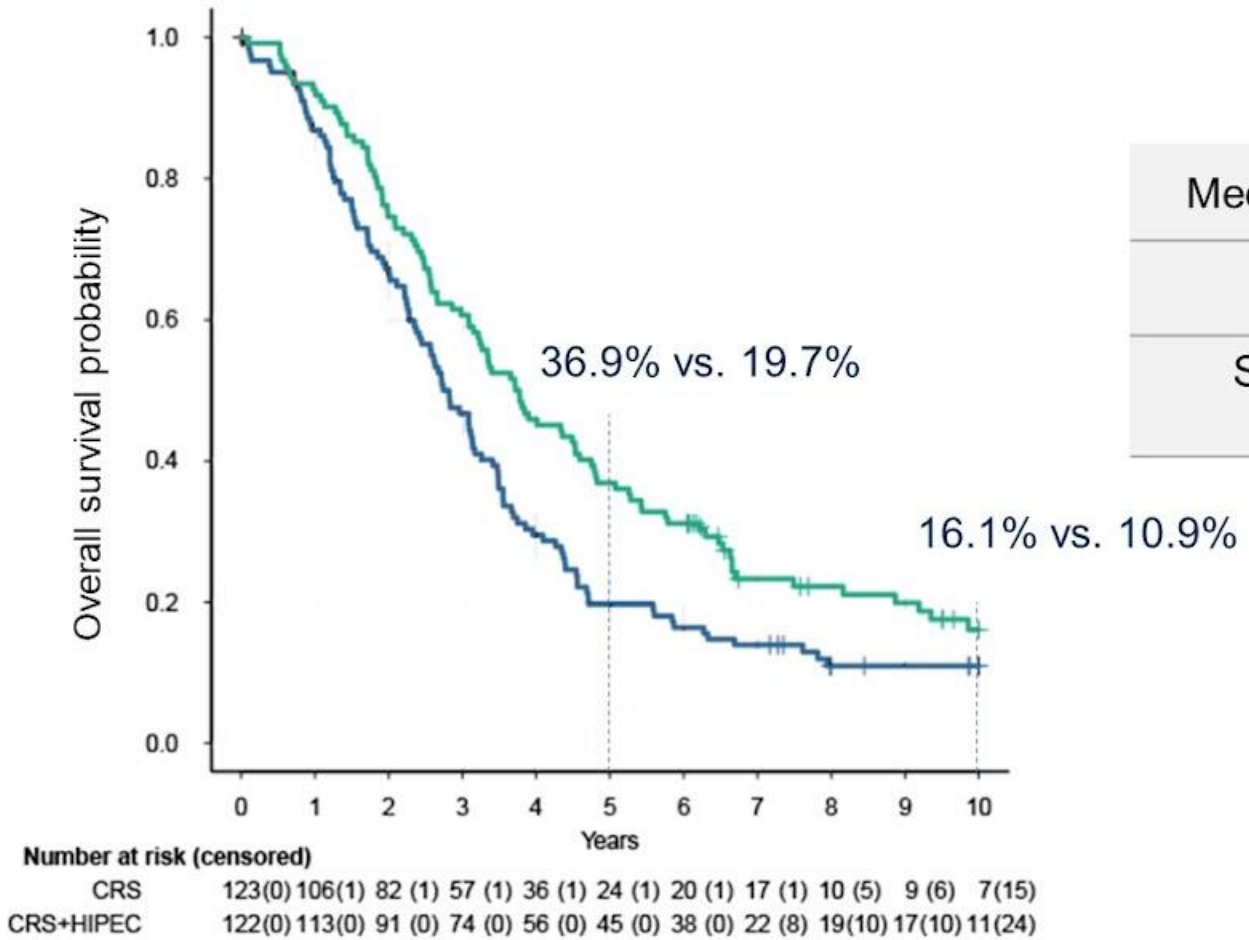
OS after ten years of follow-up



	CRS-HIPEC	CRS
Median OS, mo	44.9	33.3
HR (95%CI)	**0.70 (0.53 – 0.92)**	
Stratified log-rank p	0.0113	

HIPEC improves long-term overall survival

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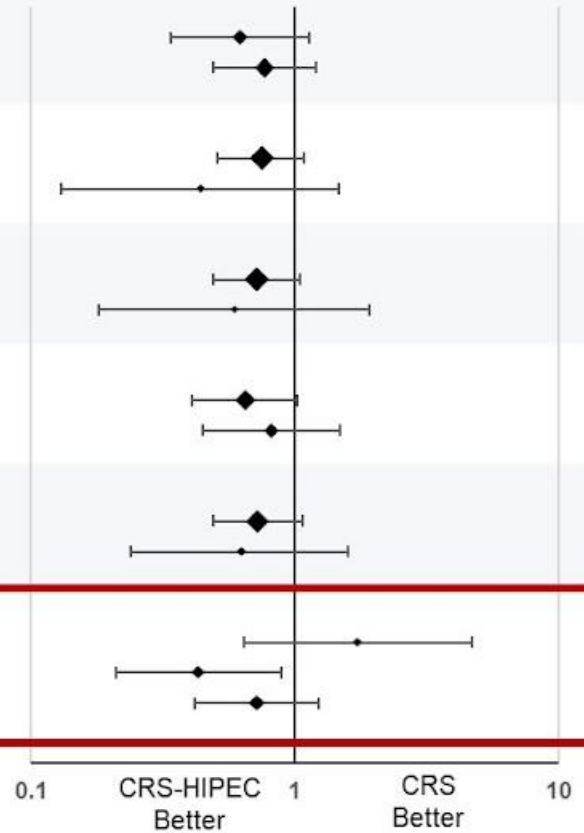
Subgroup analyses – OS

	CRS	CRS-HIPEC	Hazard Ratio (99% CI)		P for interaction
Age					0.4739
≥65 yr	42/45	33/43	0.62	(0.34-1.14)	
<65 yr	66/78	67/79	0.77	(0.49-1.21)	
Histologic type					0.2306
High-grade serous	94/107	91/112	0.75	(0.51-1.09)	
Other	14/15	8/9	0.44	(0.13-1.47)	
Prior suboptimal CRS					0.7212
No	97/111	91/110	0.72	(0.49-1.05)	
Yes	11/12	9/12	0.59	(0.18-1.91)	
No. of involved regions					0.3255
0 – 5	7/83	61/83	0.65	(0.41-1.02)	
6 – 8	38/40	39/39	0.82	(0.45-1.48)	
Laparoscopy before surgery					0.6616
No	92/105	85/103	0.72	(0.49-1.07)	
Yes	16/18	15/19	0.63	(0.24-1.60)	
HRD/HRP[1]					0.0159
gBRCA1/2 or sBRCA1/2	12/18	15/16	1.73	(0.64-4.72)	
BRCA1like/BRCAwt	34/35	23/30	0.43	(0.21-0.89)	
Non-BRCA1like/BRCAwt	49/53	43/48	0.72	(0.42-1.23)	



Exploratory subgroup analysis suggests that the BRCA1like/BRCAwt group derives most benefit from HIPEC. This finding warrants further evaluation

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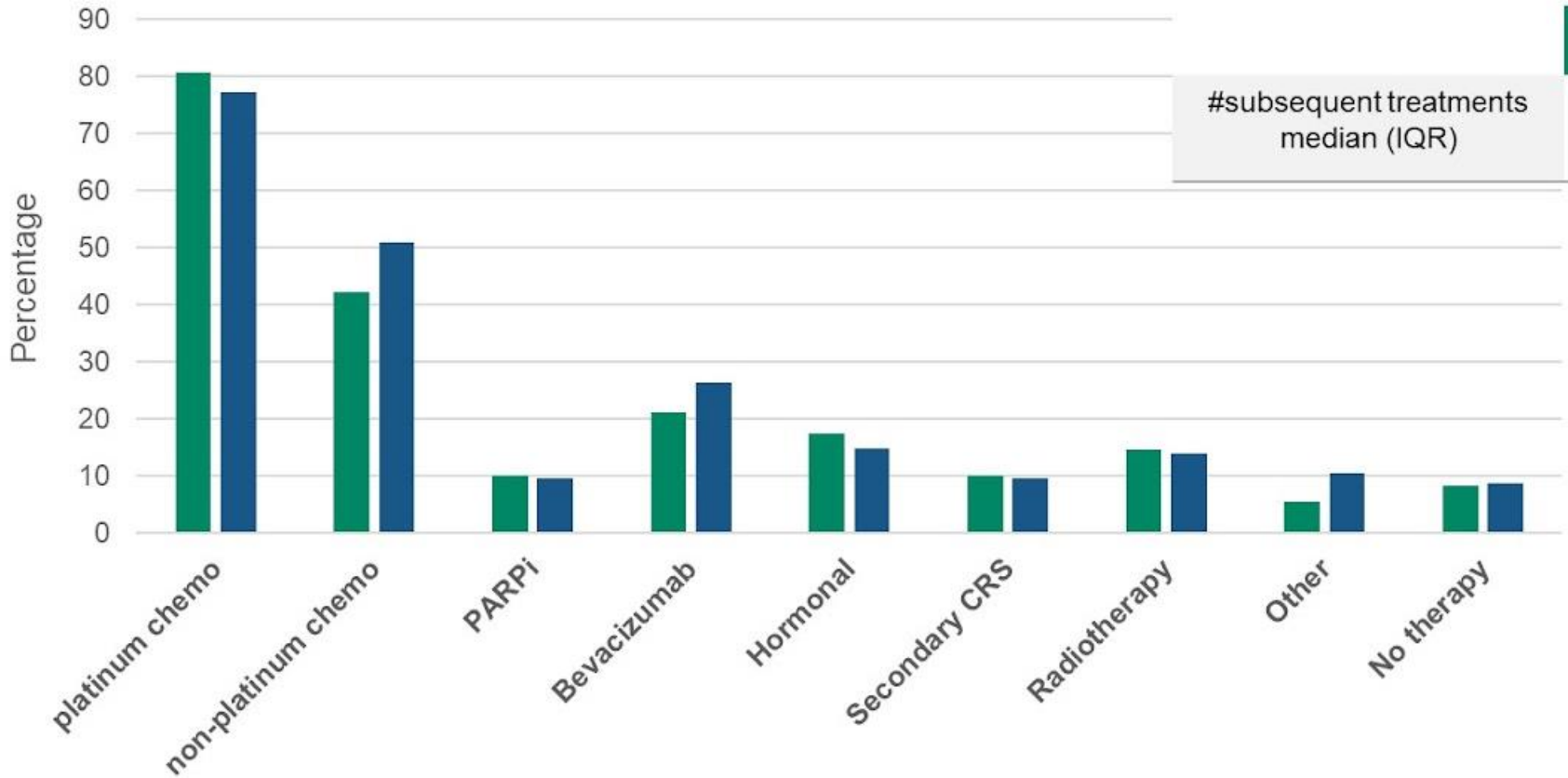
Therapies for recurrence



	CRS-HIPEC	CRS
#subsequent treatments median (IQR)	2 (1-3)	2 (1-3)

No significant difference in the use of subsequent therapies for recurrences

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2023 ASCO ANNUAL MEETING

unicancer

Hyperthermic intraperitoneal chemotherapy in platinum-sensitive relapsed epithelial ovarian cancer: The CHIPOR randomized phase III trial

Jean-Marc Classe, Pierre Meeus, Eric Leblanc, Romuald Wernert, Francois Quenet, Frédéric Marchal, Gilles Houvenaeghel, Anne-Sophie Bats, Gwenael Ferron, Cecile Brigand, Dominique Berton, Laurence Gladieff, Florence Joly, Isabelle Laure Ray-Coquard, Sylvaine Durand-Fontanier, Gabriel Liberale, Emilie Brument, Bernard Asselain, Loïc Campion, Olivier Glehen

Institut de Cancérologie Ouest, Nantes; Centre Léon Bérard, Lyon; Centre Oscar Lambret, Lille; Institut de Cancérologie Ouest, Angers; ICM Val d'Aurelle, Montpellier; Institut de Cancerologie de Lorraine, Vandoeuvre-Lès-Nancy; Institut Paoli Calmettes, Marseille; Hôpital Européen Georges Pompidou, Paris; Institut Claudius Regaud, IUCT-Oncopole, Toulouse; CHU Hautepierre, Strasbourg; Institut de Cancérologie Ouest, Nantes; Institut Claudius Regaud, IUCT-Oncopole Toulouse Francois Baclesse Cancer Center, Caen; CHU Dupuytren, Limoges, France; Institut Jules Bordet, Bruxelle, Belgium; UCGI, Prodige Intergroup, UNICANCER, Paris; ARCAGY-GINECO, Paris; Institut de Cancérologie Ouest, Nantes; Lyon Hopital Universitaire, Pierre-Bénite, France

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CHIPOR trial (NCT01376752): Multicenter randomized phase III trial

- First relapse of epithelial ovarian cancer
- PFI ≥6 months
- Response to 6 cycles of platinum-based chemotherapy
- Complete surgery achievable

N=415

Median laparotomy
Complete resection

SURGERY

CC0/1

Randomization during surgery

R 1:1

HIPEC
(cisplatin 75 mg/m² 41°C for 60 min)
n=207

No HIPEC
n=208

SOC maintenance therapy

Stratification:
- **Center**
- **Residual disease (none vs <0.25 cm)**

- Primary endpoint: **OS**
- Secondary endpoint: **PFS, TTST, safety, surgical outcome, QoL**
- Median follow up 6.2 years

[a]Added Oct 8, 2020 CC0 = -free interval; SOC = standard of care

CHIPOR trial: Baseline (pre-randomization) characteristics

Characteristics	No HIPEC (n=208)	HIPEC (n=207)
Median age (IQR), years	**59** (53–67)	**62** (55–68)
FIGO stage III/IV at primary treatment, %	84%	88%
Bevacizumab (first-line setting), n (%)	73 (35%)	64 (31%)
Median PFI (IQR), months	**17.8** (11.8–25.3)	**17.4** (10.6–26.6)
High-grade serous or grade 3 endometrioid, n (%)[a]	165 (82%)	159 (79%)
Completed 6 cycles of chemotherapy, n (%)	189 (91%)	188 (91%)
Surgery to CC0, n (%)	**180 (87%)**	**180 (87%)**

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CHIPOR trial: Severe morbidity and mortality (within 30 days after surgery)

No. of patients (%)	No HIPEC (n=208)	HIPEC (n=207)
Median duration of surgery (IQR), min	218 (160–282)	337 (272–407)
Digestive tract resection	78 (38%)	85 (41%)
Stoma diversion	10 (4.8%)	20 (9.7%)
Grade ≥3 morbidity	35 (17%)	72 (35%)
Mortality	3 (1.4%)	0

CHIPOR trial: Kidney failure

No. of patients (%)	No HIPEC (n=208)	HIPEC (n=207)
Severe kidney failure	3 (1.4%)	21 (10%)
Before thiosulfate amendment[a]	1/154 (0.7%)	19/156 (12%)
After thiosulfate amendment[a]	2/54 (3.7%)	2/51 (3.9%)

[a]Thiosulfate amendment, June 2018

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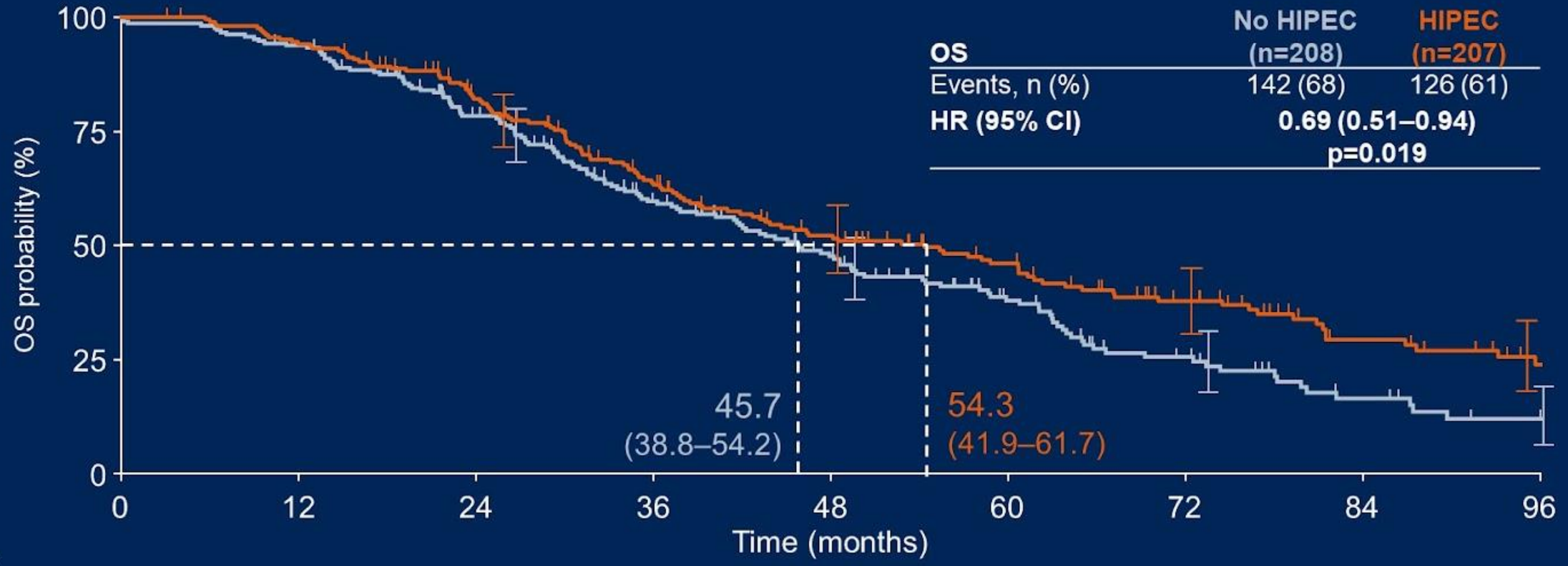
CHIPOR trial: Primary endpoint (OS, ITT population)



OS	No HIPEC (n=208)	HIPEC (n=207)
Events, n (%)	142 (68)	126 (61)
HR (95% CI)	**0.69 (0.51–0.94)**	
	p=0.019	

No. at risk								
HIPEC	207	193	158	113	87	65	44	25	15
No HIPEC	208	194	150	106	75	48	27	13	7

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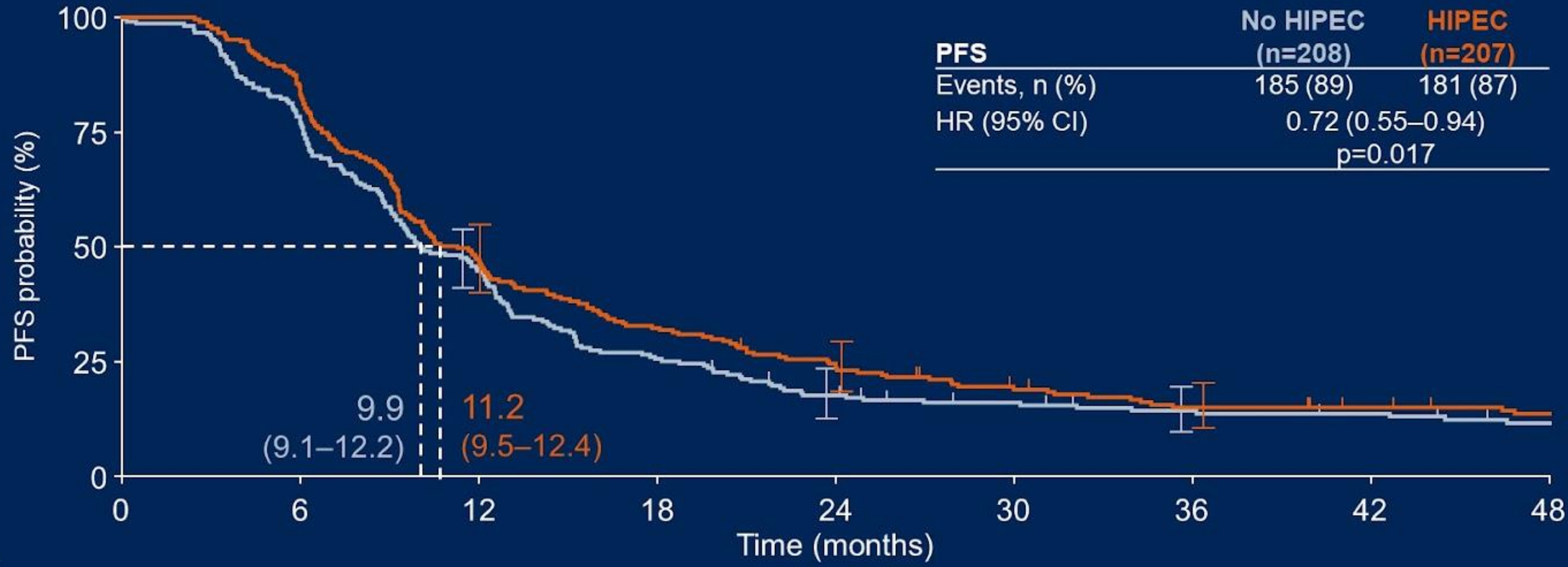
CHIPOR trial: PFS (secondary endpoint)



PFS	No HIPEC (n=208)	HIPEC (n=207)
Events, n (%)	185 (89)	181 (87)
HR (95% CI)	0.72 (0.55–0.94) p=0.017	

No. at risk									
HIPEC	207	172	97	67	48	35	27	24	20
No HIPEC	208	160	93	53	34	28	23	21	16

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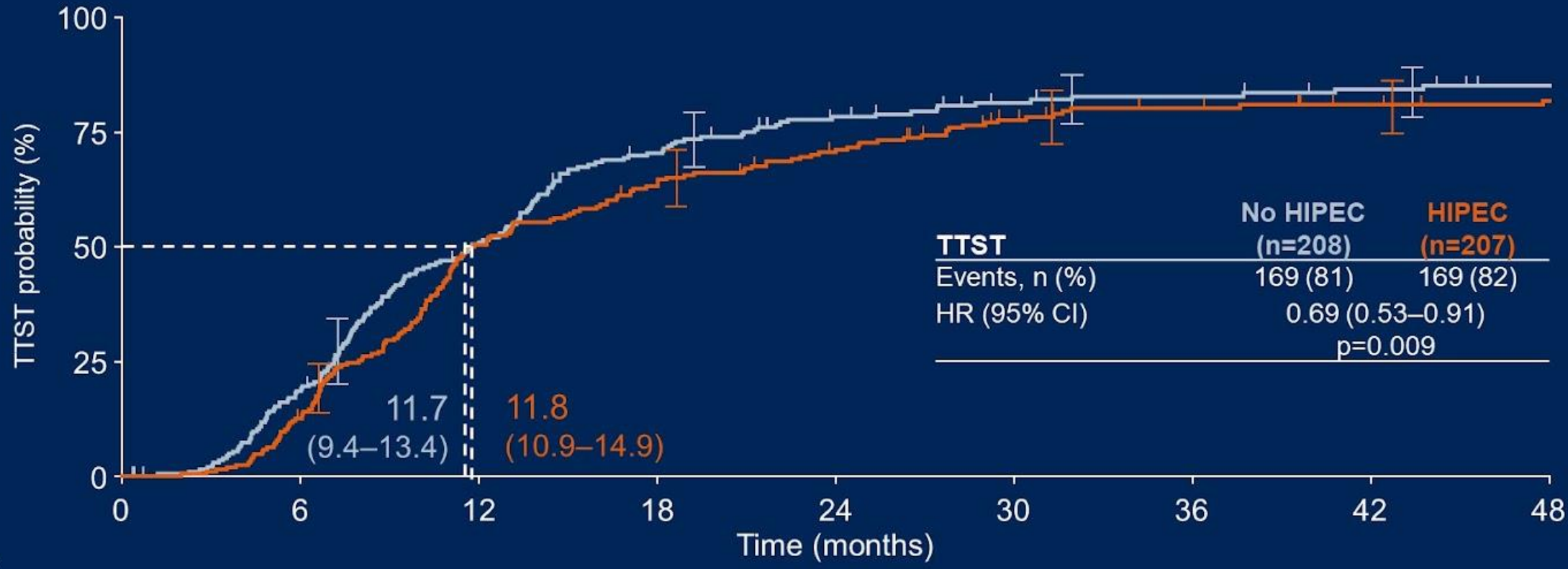
CHIPOR trial: TTST (secondary endpoint)



TTST	No HIPEC (n=208)	HIPEC (n=207)
Events, n (%)	169 (81)	169 (82)
HR (95% CI)	0.69 (0.53–0.91) p=0.009	

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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 Trillsch,[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 Aghajanian[20]

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

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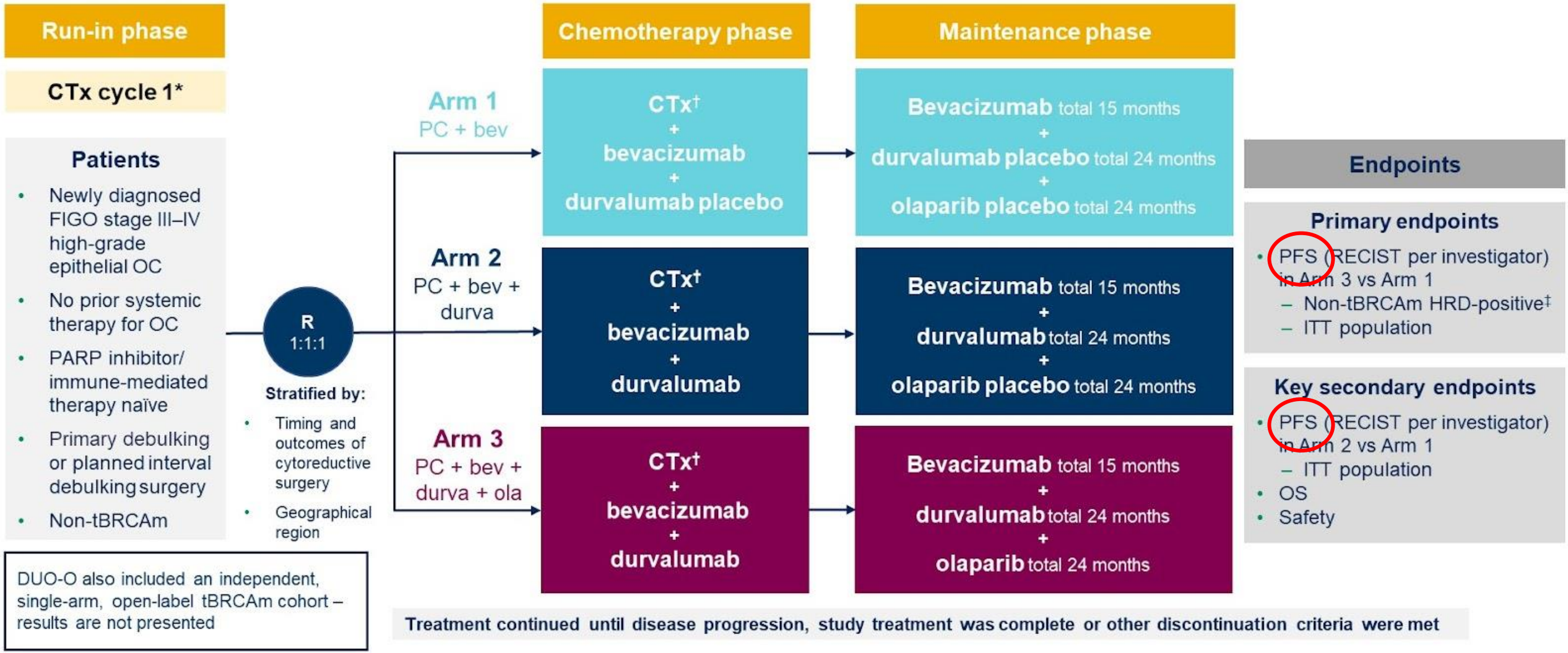
DUO-O study design



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Patient characteristics

Characteristics		Arm 1 PC + bev N=378	Arm 2 PC + bev + durva N=374	Arm 3 PC + bev + durva + ola N=378
Age, years	Median age (range)	59.0 (32–83)	58.0 (29–85)	61.0 (21–84)
Geographical region,* %	Europe	66	66	66
	North America	12	12	12
	Rest of world	22	22	22
FIGO stage,† %	III	63	69	67
	IV	37	31	33
ECOG status, %	0	64	69	69
	1	36	31	31
Histology, %	High-grade serous	88	87	90
	Clear cell	5	6	3
	High-grade endometrioid	3	2	2
	Other‡	4	5	5

Characteristics		Arm 1 PC + bev N=378	Arm 2 PC + bev + durva N=374	Arm 3 PC + bev + durva + ola N=378
Surgery status at study entry, %	Upfront primary surgery	58	59	63
	Planned IDS	42	41	37
Timing and outcome of cytoreductive surgery (as per stratification),* %	No macroscopic residual disease after upfront surgery	38	38	38
	Macroscopic residual disease after upfront surgery **OR** Planned interval debulking surgery	62	62	62
HRD status,§ %	HRD-positive	38	40	37
	HRD-negative	57	53	56
	Unknown	5	7	7

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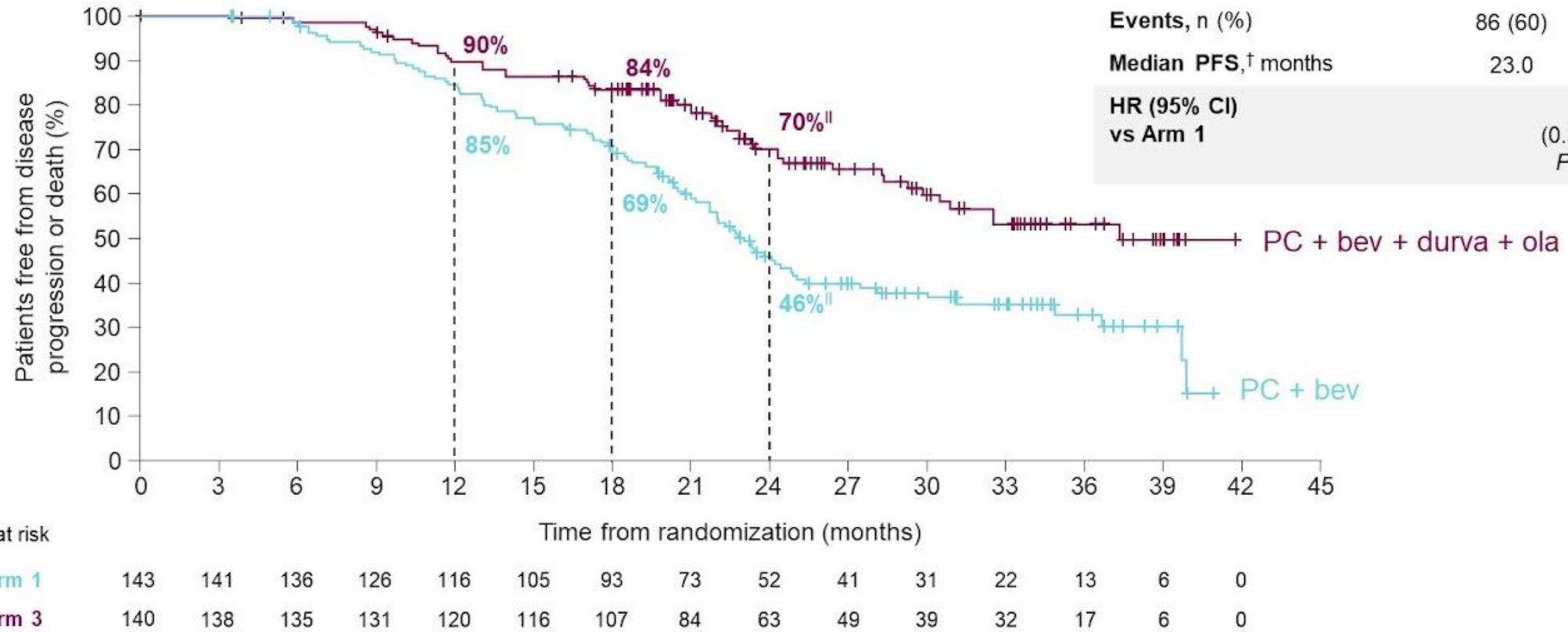
PFS: Non-tBRCAm HRD-positive population

Arm 3 vs Arm 1

	Arm 1 PC + bev N=143	Arm 3 PC + bev + durva + ola N=140
Median follow-up,* months	28.8	25.6
Events, n (%)	86 (60)	49 (35)
Median PFS,† months	23.0	37.3‡
HR (95% CI) vs Arm 1	**0.49** (0.34–0.69)§ *P*<0.0001	



Patients at risk

Arm 1	143	141	136	126	116	105	93	73	52	41	31	22	13	6	0
Arm 3	140	138	135	131	120	116	107	84	63	49	39	32	17	6	0

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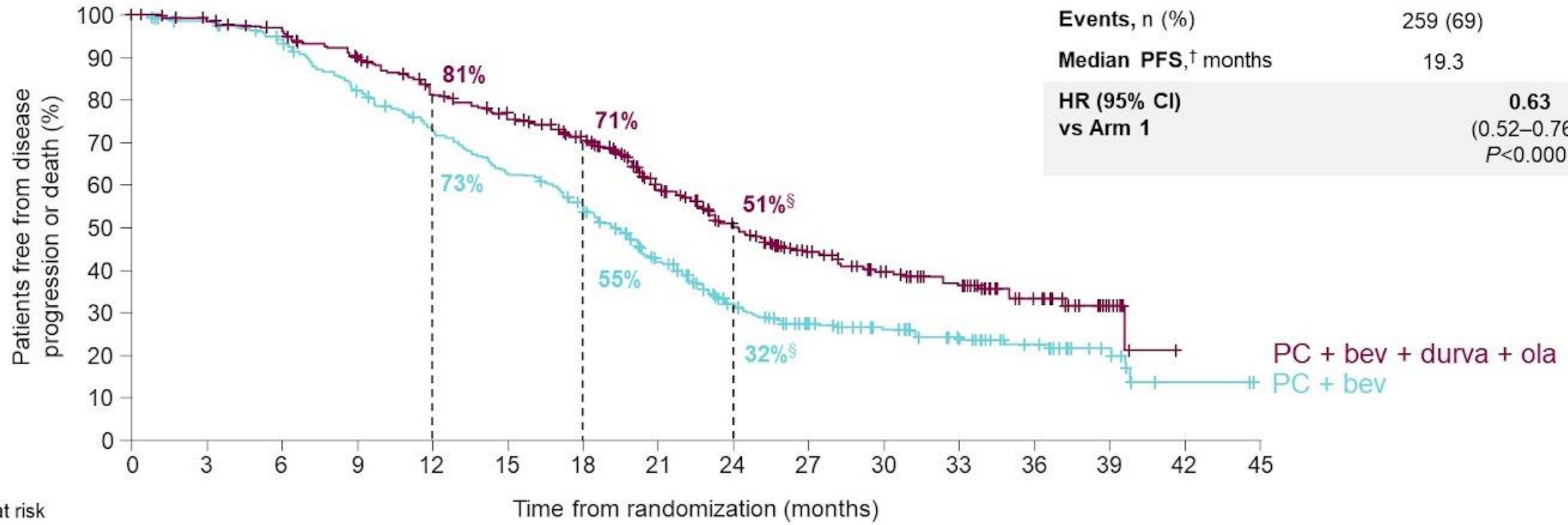
PFS: ITT population
Arm 3 vs Arm 1

	Arm 1 PC + bev N=378	Arm 3 PC + bev + durva + ola N=378
Median follow-up,* months	25.5	23.3
Events, n (%)	259 (69)	193 (51)
Median PFS,† months	19.3	24.2
HR (95% CI) vs Arm 1	**0.63** (0.52–0.76)‡ *P*<0.0001	



Patients at risk

Arm 1	378	363	341	297	260	223	189	130	87	63	51	35	23	11	2	0
Arm 3	378	366	351	323	286	266	228	163	123	84	65	52	27	9	0	

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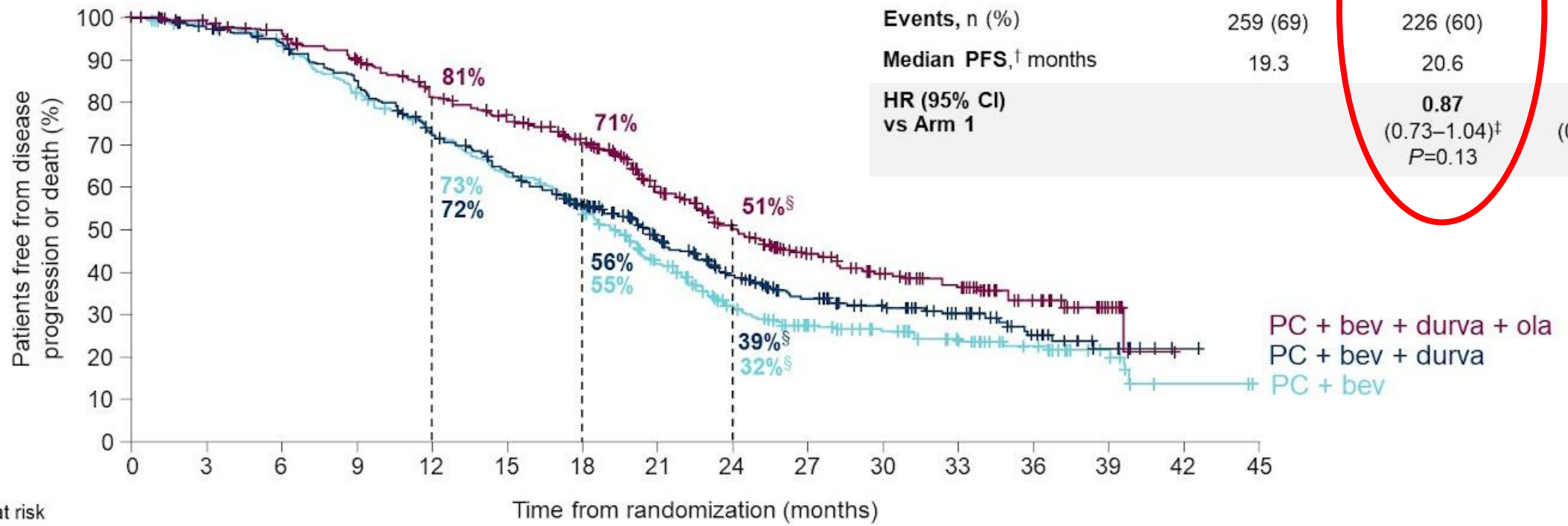
PFS: ITT population

	Arm 1 PC + bev N=378	Arm 2 PC + bev + durva N=374	Arm 3 PC + bev + durva + ola N=378
Median follow-up,* months	25.5	23.1	23.3
Events, n (%)	259 (69)	226 (60)	193 (51)
Median PFS,† months	19.3	20.6	24.2
HR (95% CI) vs Arm 1		**0.87** (0.73–1.04)‡ *P*=0.13	**0.63** (0.52–0.76)‡ *P*<0.0001



Patients at risk

Arm 1	378	363	341	297	260	223	189	130	87	63	51	35	23	11	2	0
Arm 2	374	354	336	301	254	221	180	130	93	70	54	39	23	11	1	0
Arm 3	378	366	351	323	286	266	228	163	123	84	65	52	27	9	0	

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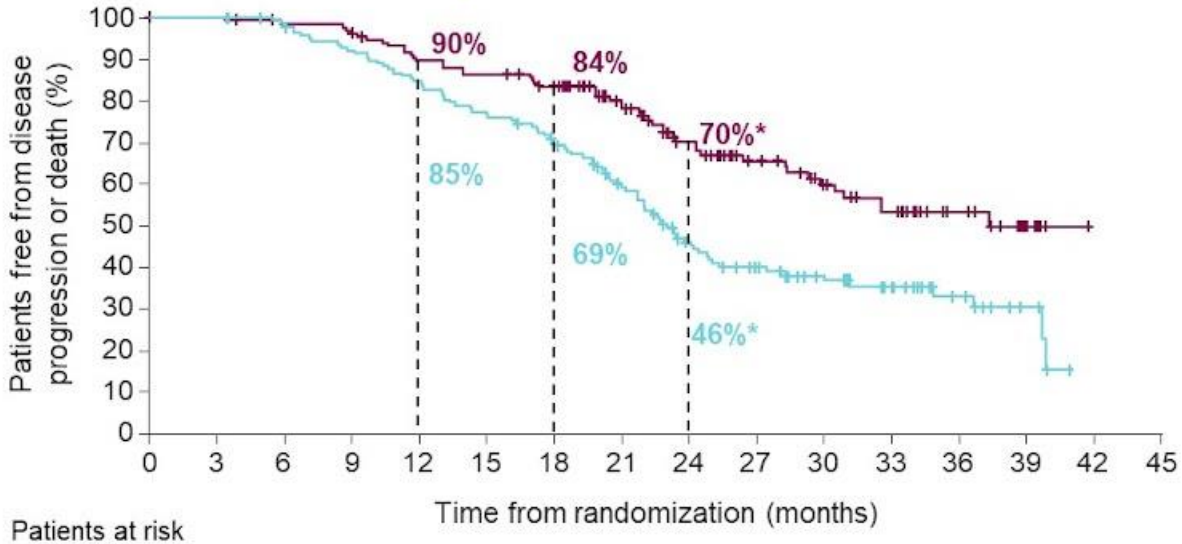
Subgroup analysis of PFS by HRD status

Non-tBRCAm HRD-positive

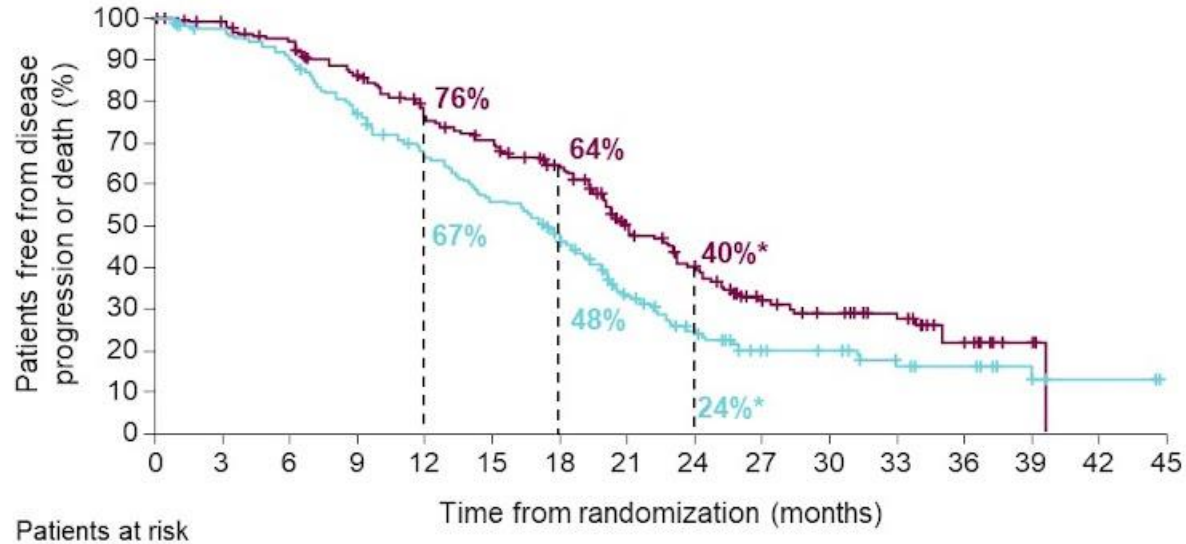


Patients at risk

Arm 1	143	141	136	126	116	105	93	73	52	41	31	22	13	6	0
Arm 3	140	138	135	131	120	116	107	84	63	49	39	32	17	6	0

	Arm 1 PC + bev N=143	Arm 3 PC + bev + durva + ola N=140
Events, n (%)	86 (60)	49 (35)
Median PFS, months†	23.0	37.3‡
HR (95% CI) vs Arm 1		**0.51** (0.36–0.72)§

HRD-negative



Patients at risk

Arm 1	216	203	188	159	135	112	92	55	34	21	19	12	9	5	2	0
Arm 3	211	202	190	169	145	132	111	75	57	33	26	20	10	3	0	

	Arm 1 PC + bev N=216	Arm 3 PC + bev + durva + ola N=211
Events, n (%)	157 (73)	127 (60)
Median PFS, months†	17.4	20.9
HR (95% CI) vs Arm 1		**0.68** (0.54–0.86)§

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Safety summary

AEs, n (%)	Overall (chemotherapy phase + maintenance phase)			Maintenance phase		
	Arm 1 PC + bev N=376	Arm 2 PC + bev + durva N=373	Arm 3 PC + bev + durva + ola N=378	Arm 1 PC + bev N=331	Arm 2 PC + bev + durva N=323	Arm 3 PC + bev + durva + ola N=336
Any-grade AE	373 (99)	371 (99)	375 (99)	308 (93)	303 (94)	328 (98)
Grade ≥3 AE	231 (61)	245 (66)	269 (71)	88 (27)	113 (35)	164 (49)
AE with outcome of death	4 (1)	9 (2)	6 (2)	2 (1)	3 (1)	4 (1)
Serious AE (including outcome of death)	128 (34)	161 (43)	148 (39)	50 (15)	91 (28)	83 (25)
AE of special interest to olaparib						
MDS/AML*	1 (<1)	0	2 (1)	1 (<1)	0	1 (<1)
New primary malignancies*	1 (<1)	1 (<1)	4 (1)	1 (<1)	1 (<1)	3 (1)
Pneumonitis	3 (1)	5 (1)	7 (2)	1 (<1)	3 (1)	6 (2)
Any immune-mediated AEs†	132 (35)	209 (56)	200 (53)	94 (28)	139 (43)	141 (42)
AEs leading to dose modification‡,§	272 (72)	299 (80)	323 (85)	163 (49)	182 (56)	254 (76)
AEs leading to discontinuation‡	77 (20)	98 (26)	131 (35)	44 (13)	54 (17)	88 (26)
AEs leading to discontinuation of PC/bevacizumab	57 (15)	59 (16)	70 (19)	27 (8)	24 (7)	35 (10)
AEs leading to discontinuation of durvalumab/placebo	24 (6)	62 (17)	65 (17)	14 (4)	39 (12)	40 (12)
AEs leading to discontinuation of olaparib/placebo	15 (4)	19 (5)	62 (16)	14 (4)	19 (6)	61 (18)

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2023 ASCO ANNUAL MEETING

Randomized controlled phase III trial of weekly paclitaxel ± ofranergene obadenovec (VB-111) for platinum-resistant ovarian cancer (OVAL Study/GOG 3018)

Rebecca C. Arend, MD, MSPH[1], Bradley J. Monk[2], Ronnie Shapira-Frommer[3], Ashley F. Haggerty[4], Edwin A. Alvarez[5], Amnon Amit[6], Angeles Alvarez Secord[7], Carolyn Muller[8], Antonio Casado Herraez[9], Thomas J. Herzog[10], Krishnansu S. Tewari[12], Joshua Cohen[13], Marilyn Huang[14], Adelya Yachnin[15], Laura Holeman[11] Jonathan A. Ledermann[16], Tamar Rachmilewitz Minei[17], Marc Buyse[18], Shifra Fain Shmueli[17], Michal Lavi[17], Dror Harats[17], Richard T. Penson[19], OVAL/GOG-3018 Investigators

1. University of Alabama at Birmingham School of Medicine, 2. HonorHealth Research Institute, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA, 3. Chaim Sheba Medical Center, Ramat Gan, Israel, 4. Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA, 5. University of California, San Francisco, CA, USA, 6. Rambam Health Care Campus, Haifa, Israel, 7. Duke Cancer Institute, Duke University Health System, Durham, NC, USA, 8. University of New Mexico, Albuquerque, NM, USA, 9. San Carlos University Teaching Hospital, Madrid, Spain, 10. University of Cincinnati Cancer Center, University of Cincinnati, Cincinnati, OH, USA, 11. Stephenson Cancer Center at the University of Oklahoma, Oklahoma City, OK, USA, 12. University of California, Medical Center, Orange, CA, USA, 13. Ronald Reagan UCLA Medical Center Los Angeles, CA, USA, 14. Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA, 15. Kaplan Medical Center, Rehovot, Israel, 16. UCL Cancer Institute, University College London, London, UK, 17. VBL Therapeutics, Modiin, Israel, 18. International Drug Development Institute, Louvain-la-Neuve, Belgium , 19. Massachusetts General Hospital, Boston, MA, USA

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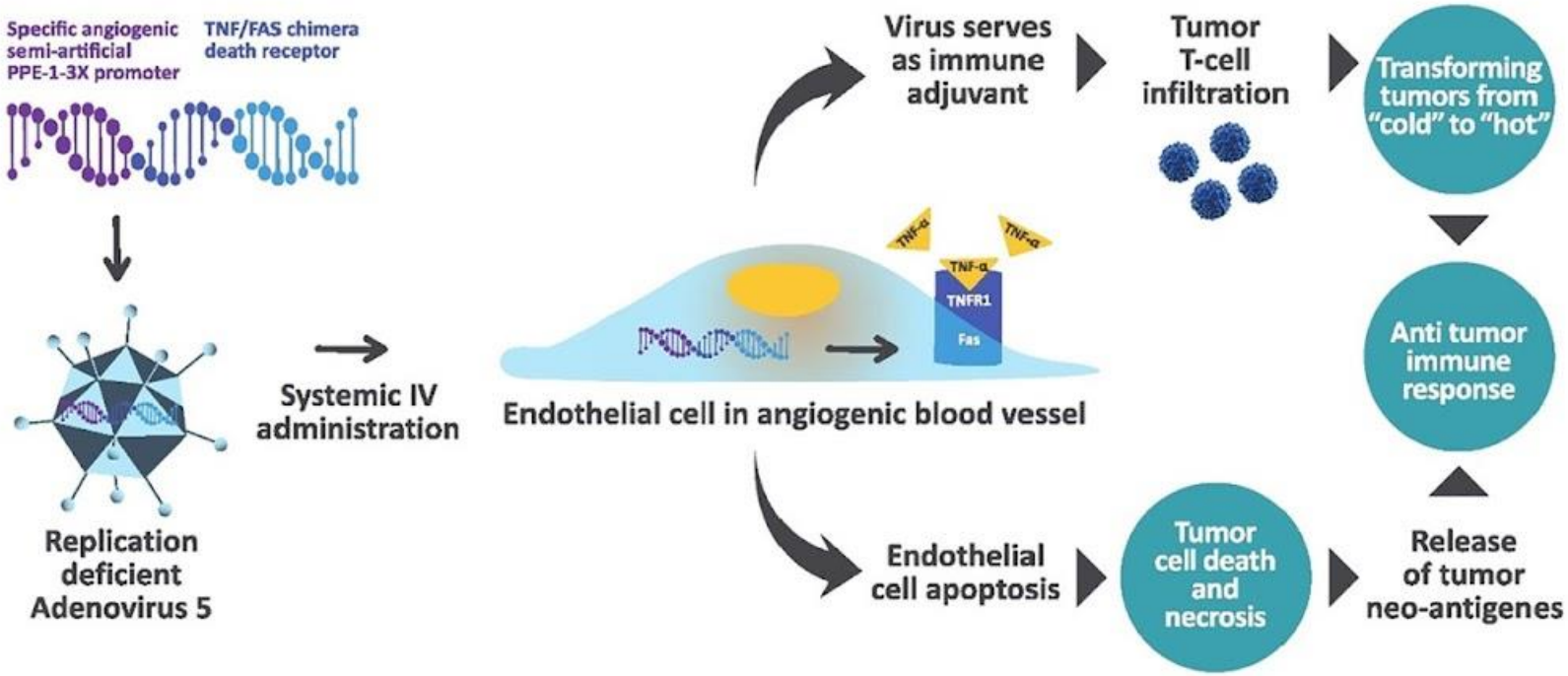
Ofranergene obadenovec (VB-111)



- 3 main components:
  - nonreplicating adenoviral vector
  - pro-endothelin 1 (PPE-1-3X) promoter
  - Fas-TNFR chimeric transgene

Arend, et. al. Gynecol. Oncol. 2020

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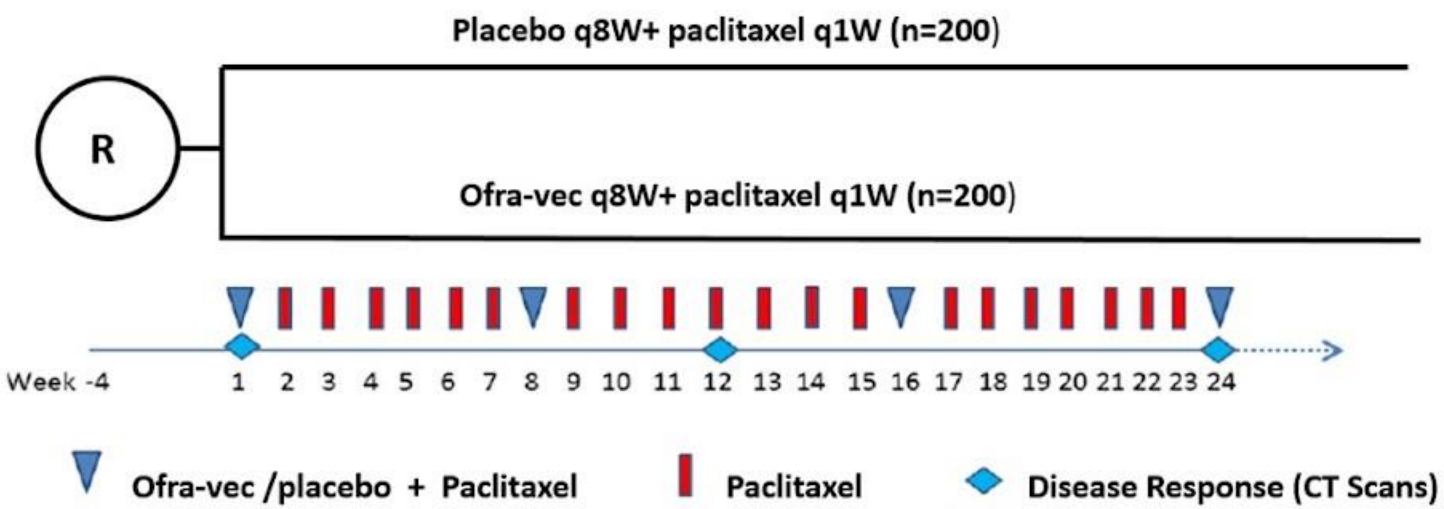
Study Design



- **Primary endpoints:** PFS, Overall Survival
- **Secondary endpoints**: ORR by CA-125 (GCIG) and RECIST 1.1 combined and individually, OS_{100}
- **Translational Scientific Objectives**: histopathology, expression, biomarkers
- Approx. 100 sites, 400 subjects
- **Clinical collaboration with the GOG Foundation, Inc.**

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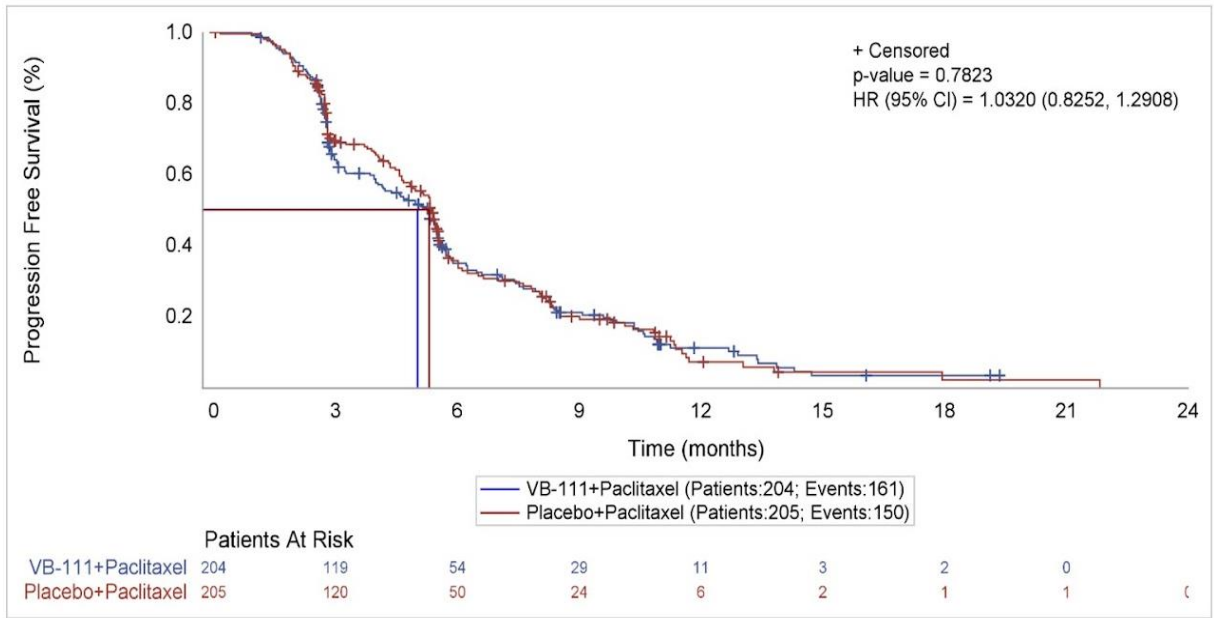
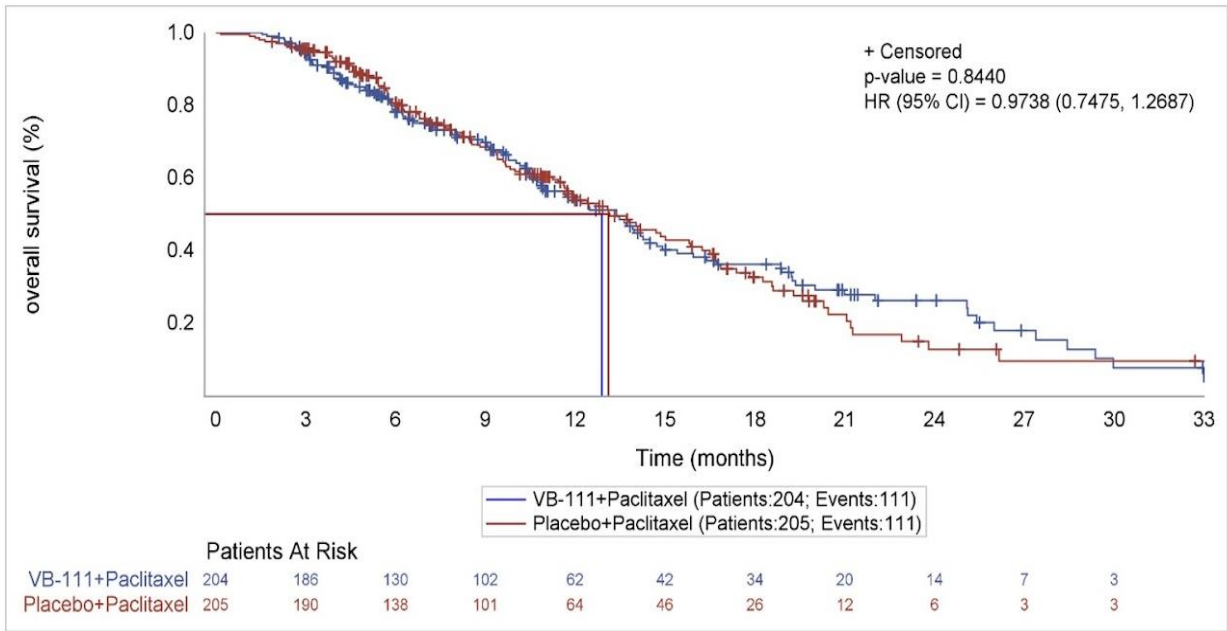
Progression Free Survival



Overall Survival



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Overall Response Rate

	ORR RECIST 1.1		ORR CA-125	
	Ofra-vec plus Paclitaxel	Placebo plus Paclitaxel	Ofra-vec plus Paclitaxel	Placebo plus Paclitaxel
N evaluable[1]	180	179	163	154
ORR (CR plus PR)	52 (28.9%)	53 (29.6%)	67 (41.1%)	76 (49.4%)
95% CI	22.76%–35.90%	23.41%–36.67%	33.8%- 48.8%	41.6%- 57.2%
p-value	0.8808		0.1403	
Best response				
CR	5 (2.8%)	4 (2.2%)	22 (13.5%)	29 (18.8%)
PR	47 (26.1%)	49 (27.4%)	45 (27.6%)	47 (30.5%)
SD/ non PR non PD	65 (36.1%)	72 (40.2%)	93 (57.1%)	75 (48.7%)
PD	59 (32.8%)	54 (30.2%)	3 (1.8%)	3 (1.9%)
NE	4 (2.2%)	–		

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2023 ASCO® ANNUAL MEETING

Luveltamab Tazevibulin (STRO-002), an Anti-Folate Receptor Alpha Antibody Drug Conjugate, Safety and Efficacy in a Broad Distribution of FOLRα Expression in Patients With Recurrent Epithelial Ovarian Cancer: Update of STRO-002-GM1 Phase 1 Dose Expansion Cohort

Ana Oaknin, Lorena Fariñas-Madrid, Carmen García-Duran, Lainie P. Martin, David M. O'Malley, Russell J. Schilder, Denise Uyar, John W. Moroney, John Paul Diaz, Alexander I. Spira, Jesus Garcia-Donas, Hatem Dokainish, Lin Liu, Craig J. Berman, R. Wendel Naumann

Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain; University of Pennsylvania, Abramson Cancer Center, Philadelphia, PA; The Ohio State University, Wexner Medical Center, Columbus, OH; Sidney Kimmel Cancer Center at Thomas Jefferson University, Philadelphia, PA; Medical College of Wisconsin, Milwaukee, WI; University of Chicago, Chicago, IL; Miami Cancer Institute, Baptist Health, Miami, FL; Virginia Cancer Specialists and US Oncology Research, Fairfax, VA; Hospital Universitario HM Sanchinarro – CIOCC, Madrid, Spain; Sutro Biopharma, Inc., South San Francisco, CA; Levine Cancer Institute, Atrium Health, Charlotte, NC

Luveltamab tazevibulin is a precisely designed (ADC) effective in targeting lower levels of FolRα-expression

SUTRO Cell-Free Platform

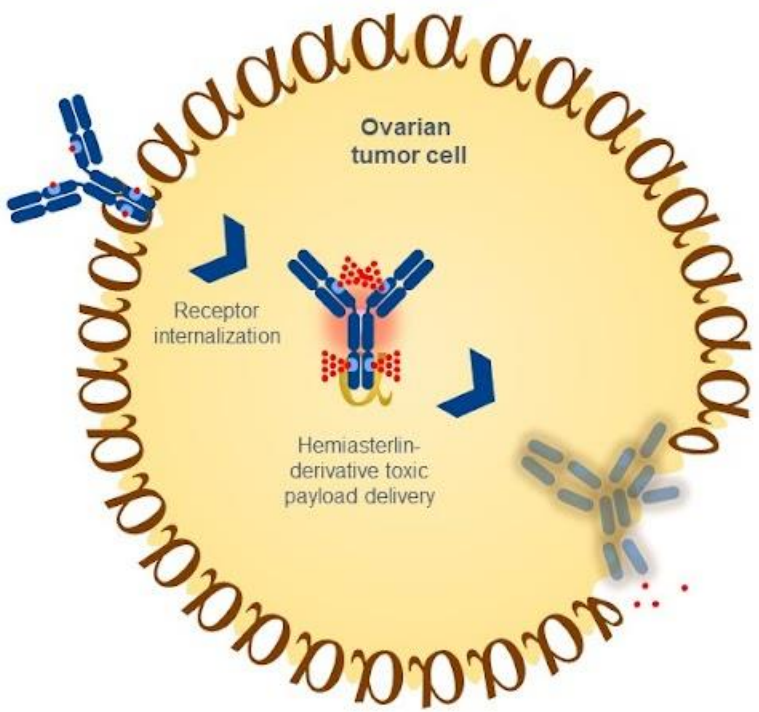
Linker-payload position

Precise, **stable position** of cathepsin B linker + tubulin-targeting hemiasterlin-derivative* payload via non-natural amino acids, optimized for **activity**

Consistent product design

Every molecule is the same, delivering consistent DAR4 payload across FolRα expression levels

Luveltamab tazevibulin or STRO-002[1]



Luveltamab Design Delivery

Cytotoxic tumor activity

Release of payload in circulation is minimized, while intratumor cell cytotoxin delivery is **efficient**

Immunogenic cell death†

Payload-induced tumor cell stress stimulates innate immune cells, helping generate **anti-tumor immunity**

Luveltamab tazevibulin is designed for optimal therapeutic index

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STRO-002-GM1: phase 1 dose expansion cohort of luveltamab tazevibulin in recurrent epithelial ovarian cancer designed to optimize dose

NCT03748186

- Recurrent disease
  - Platinum resistant
    1–3 prior regimens or
    platinum-sensitive
    2–3 prior regimens
- Fresh or archival tissue required
- No mandate for FolRα expression
- At least 1 target lesion

N=44

R
1:1

Luveltamab
4.3 mg/kg Q3W
n=23

Luveltamab
5.2 mg/kg Q3W
n=21

- Primary endpoint: ORR by RECIST v1.1
- Secondary endpoints: Safety, PK, PFS, DOR

- FolRα expression was determined retrospectively after enrollment
- FolR1 IHC assay (Ventana Medical Systems) using tumor proportion score (TPS)
- Dose reductions required for grade 4 neutropenia regardless of whether it was reported as an AE
- Growth factors allowed per institutional standard of care
- Ophthalmologist assessment for potential ocular AEs at baseline and every 2 cycles
  - No requirement for prophylactic ocular corticosteroids or antibiotics

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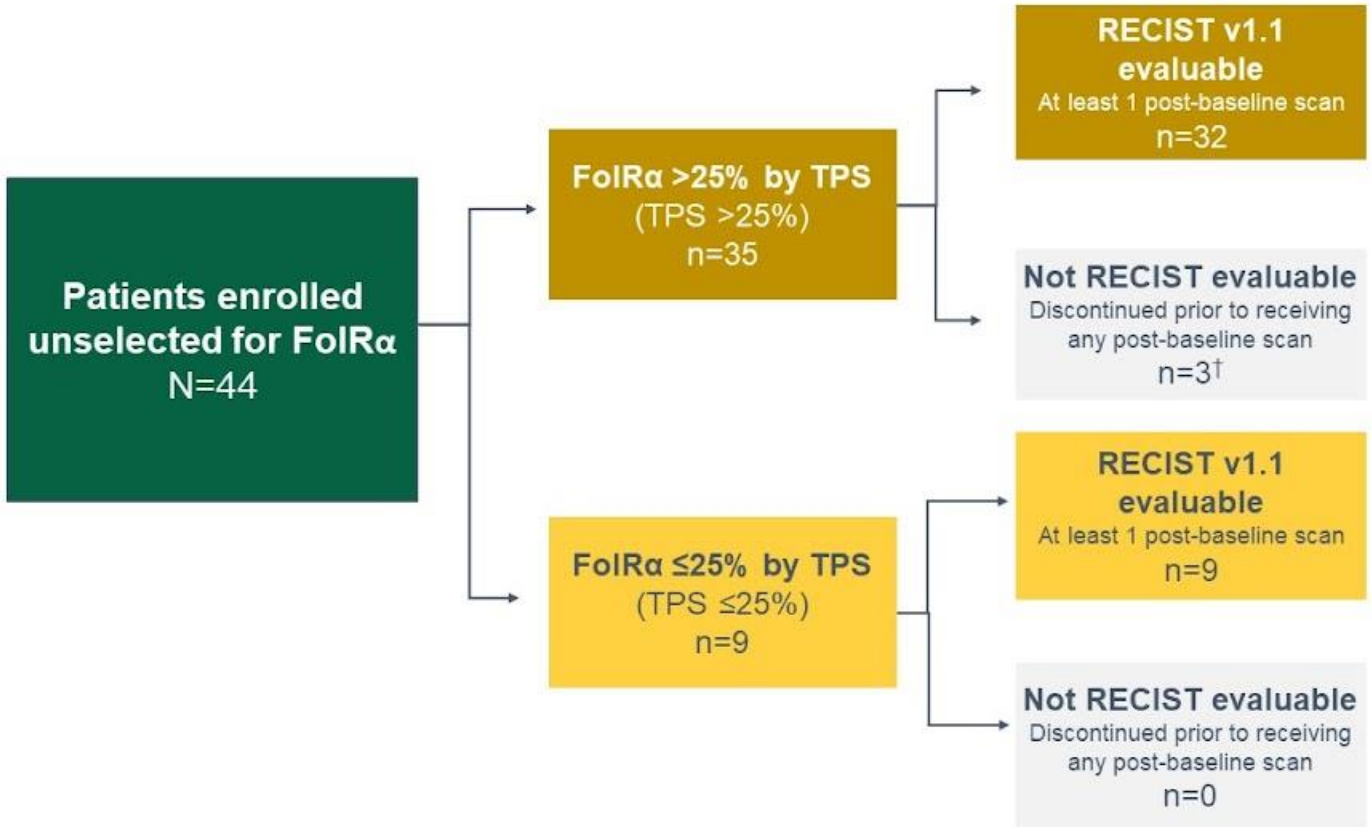
Analysis populations include all comers (unselected for FolRα) and FolRα selected (TPS >25%)

- FolRα expression retrospectively determined using IHC* on fresh or archival tissue required
- TPS is the percentage of cells stained positive at any intensity
  - Established in multiple approvals and tumor indications
  - Does not require differentiation between staining intensity
  - Simple and straightforward for pathology read
- **Enriched population defined as TPS >25%**
- **TPS >25% in 35/44 (80%) of all enrolled patients**



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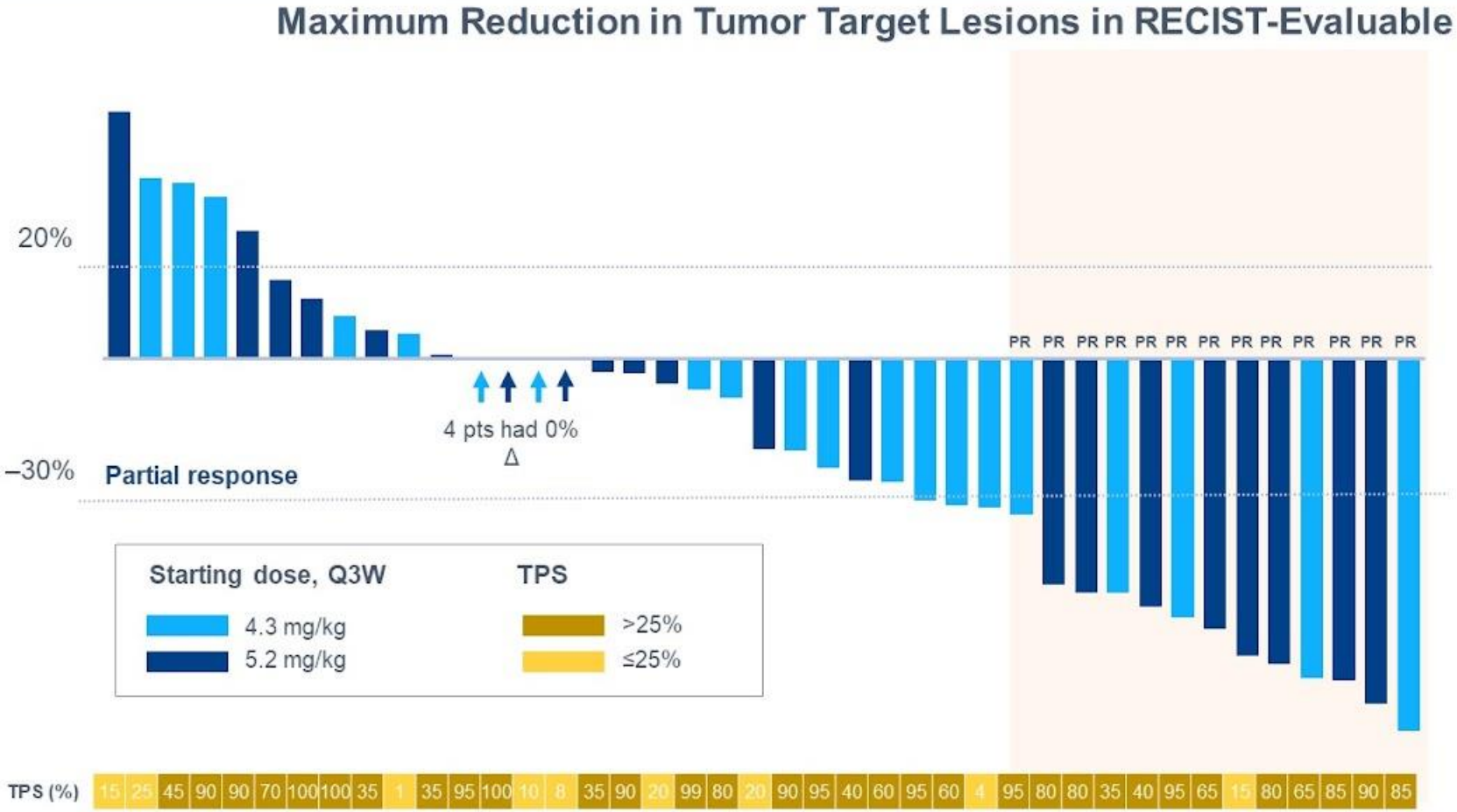
All-comers patient population (FolRα-unselected) demonstrated an ORR of 32% per RECIST v1.1



ORR: 31.7% in unselected pts

- 37.5% for FoLRα >25% by TPS

Disease control rate: 78% in unselected pts

- 81% for FolRα >25% by TPS

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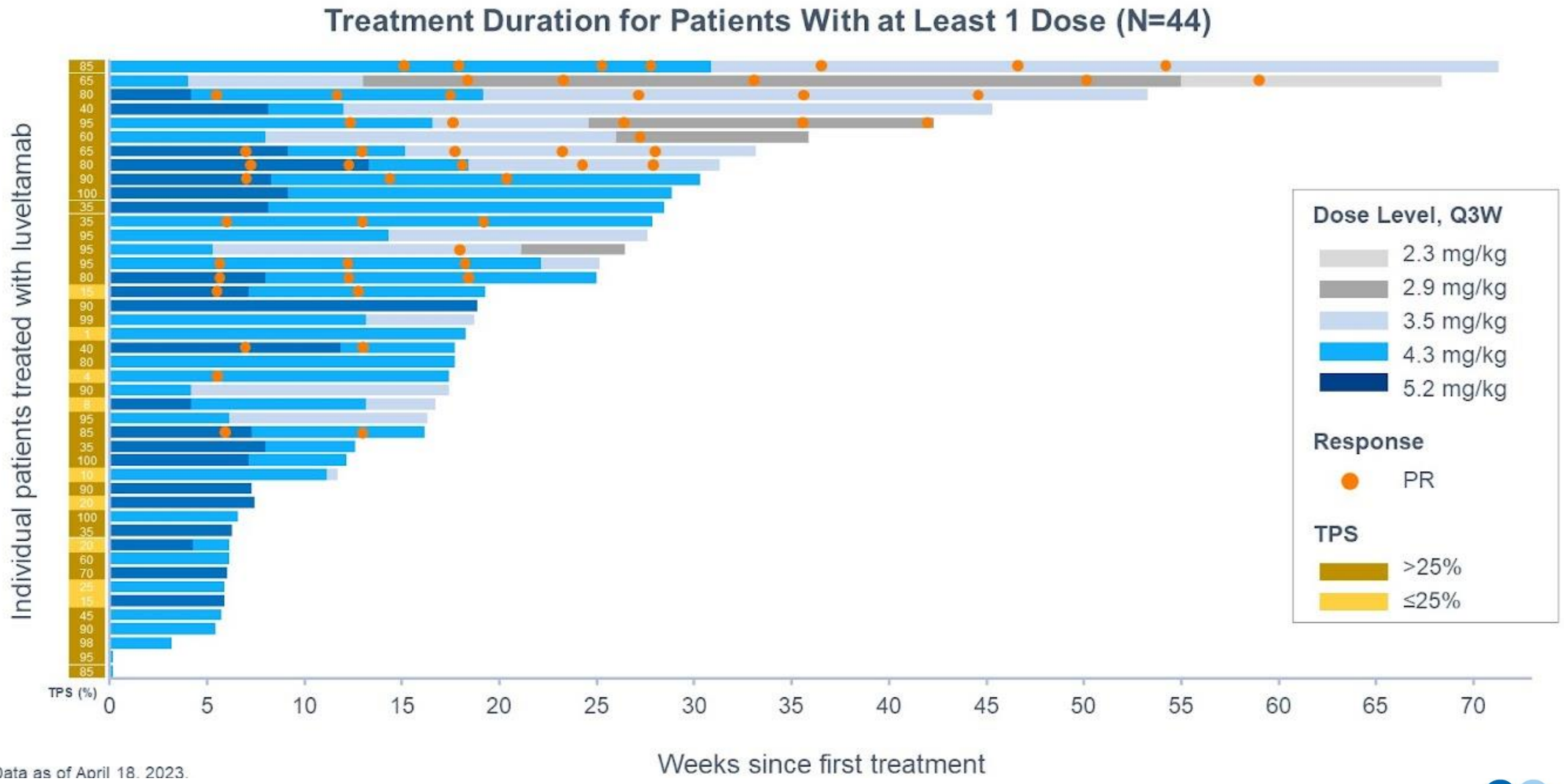
Patient responses occurred at both dose levels and were maintained with dose reductions



Data as of April 18, 2023.

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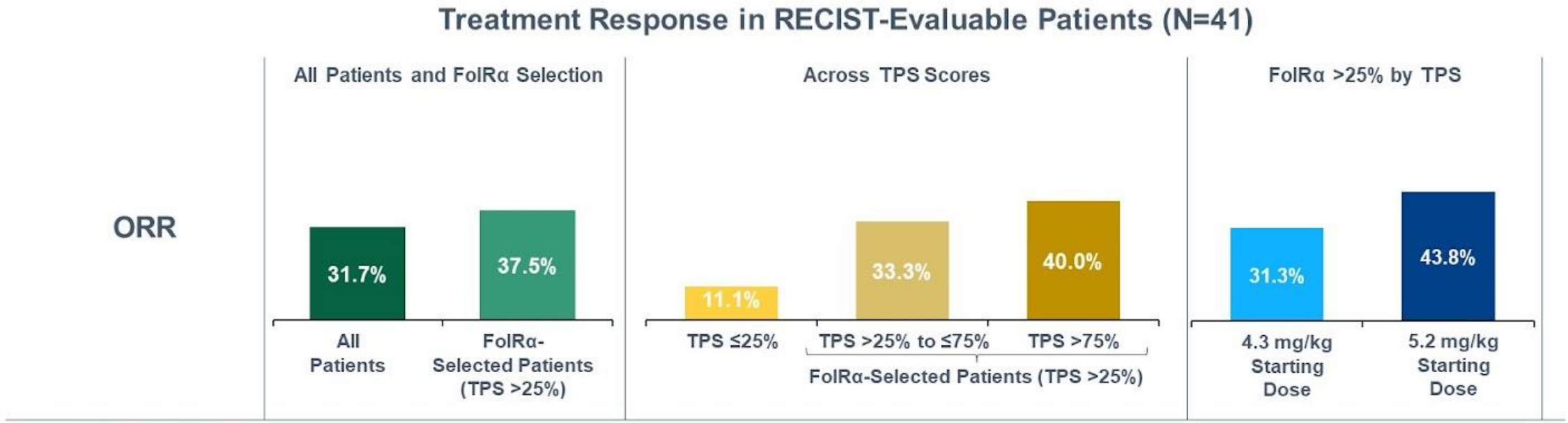
Clinical activity seen at both doses across a broad range of FolRα expression levels



RECIST-evaluable patients	N=41	n=32	n=9	n=12	n=20	n=16	n=16
PR	13	12	1	4	8	5	7
ORR (95% CI), %	**31.7 (18.1, 48.1)**	**37.5 (21.1, 56.3)**	**11.1 (0.3, 48.3)**	**33.3 (9.9, 65.1)**	**40.0 (19.1, 63.9)**	**31.3 (11.0, 58.7)**	**43.8 (19.8, 70.1)**

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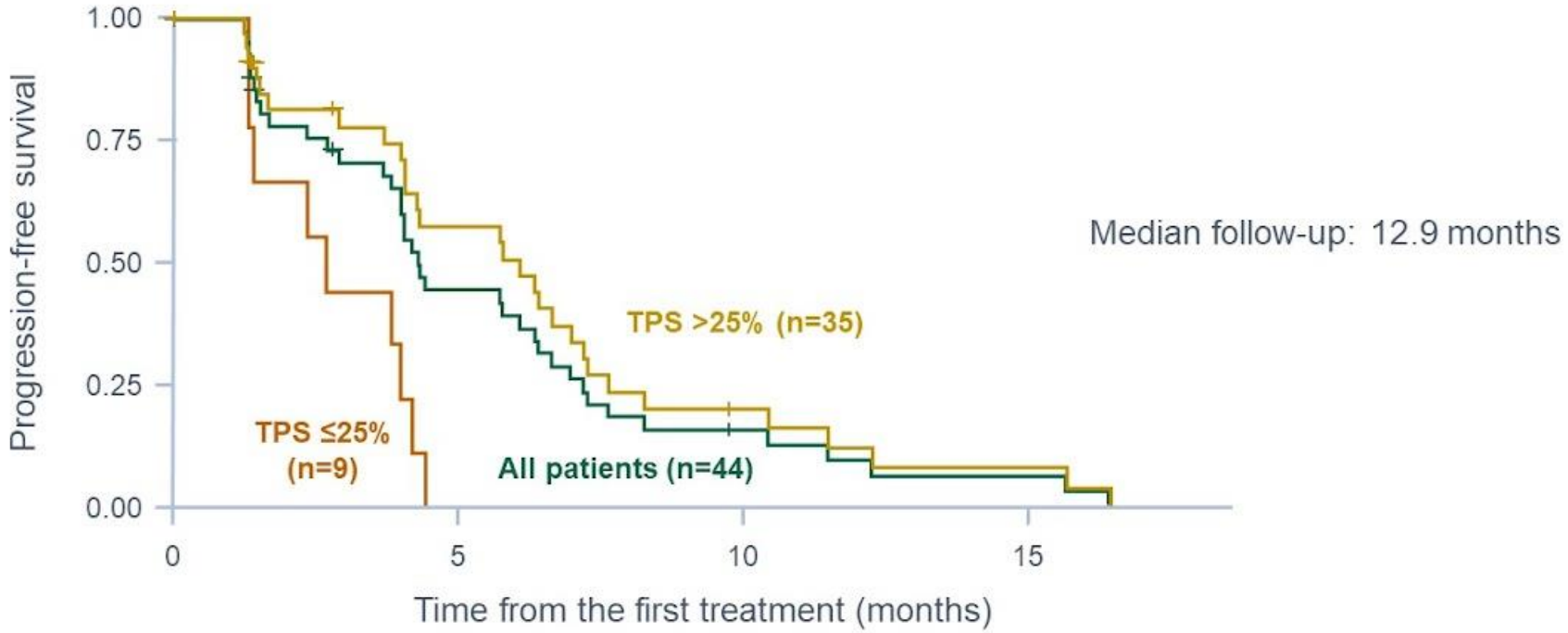
Luveltamab resulted in PFS of 6.1 months and median DOR of 5.5 months in the FolRα selected population (TPS >25%)



	All Patients (N=44)	FolRα ≤25% by TPS (n=9)	FolRα >25% by TPS (n=35)
Median DOR (range), months	5.4 (2.9, 11.0)	2.9 (NA)*	5.5 (2.5, 11.0)
Median PFS (95% CI), months	4.3 (3.8, 6.3)	2.7 (1.3, 4.2)	6.1 (4.1, 7.2)

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The TEAEs were predictable and manageable

TEAEs leading to dose reduction in 61.4%

- Neutropenia* in 17 patients (39%)
  - Primarily G3/4 uncomplicated (abnormal lab value only)
  - Febrile neutropenia in 2 patients (4.5%)
  - Resolved without growth factor support in most patients
  - Median duration of G3+ AEs, 8 days
- Arthralgia in 8 patients (18%)
- Peripheral neuropathy in 3 patients (6.8%)
  - Mostly G1/2

TEAEs leading to dose discontinuation in 3 patients (6.8%)

- G3 fatigue
- G2 neuropathy†
- G5 sepsis

Phase 2/3 REFRaME study is planned to begin with a randomized, run-in dose confirmation phase:
25 patients will be evaluated at the 5.2 mg/kg dose with **pegfilgrastim delivered prophylactically** for 2 cycles followed by a step-down dose to 4.3 mg/kg.

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Phase III MIRASOL (GOG 3045/ENGOT-ov55) Study: Mirvetuximab Soravtansine vs. Investigator's Choice of Chemotherapy in Platinum-Resistant, Advanced High-Grade Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancers with High Folate Receptor-Alpha (FRα) Expression

Kathleen N. Moore[1], Antoine Angelergues[2], Gottfried E. Konecny[3], Susana Banerjee[4], Sandro Pignata[5], Nicoletta Colombo[6], John Moroney[7], Casey Cosgrove[8], Jung-Yun Lee[9], Andrzej Roszak[10], Shani Breuer[11], Jacqueline Tromp[12], Diana Bello Roufai[13], Lucy Gilbert[14], Rowan Miller[15], Tashanna Myers[16], Yuemei Wang[17], Anna Berkenblit[17], Domenica Lorusso[18], Toon Van Gorp[19]

[1]Stephenson Cancer Center University of Oklahoma College of Medicine, Oklahoma City, OK, USA; [2]Groupe Hospitalier Diaconesses Croix Saint Simon, Paris, France; [3]UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; [4]The Royal Marsden NHS Foundation Trust - Royal Marsden Hospital, London, UK; [5]Istituto Nazionale Tumori- G. Pascale, Naples, Italy; [6]European Institute of Oncology IRCCS, Milan, Italy and University of Milan-Bicocca, Milan, Italy; [7]The University of Chicago, Chicago, IL, USA; [8]The Ohio State University, Columbus, OH, USA; [9]Severance Hospital, Seoul, South Korea; [10]Wielkopolskie Centrum Onkologii, Poznan, Poland; [11]Hadassah Ein Kerem – Sharett, Jerusalem, Israel; [12]Amsterdam UMC, Amsterdam, The Netherlands; [13]Hopital Rene Huguenin, Institut Curie, Saint-Cloud, France; [14]McGill University Health Centre, Montreal, Canada; [15]University College London Hospital, London, UK; [16]Baystate Medical Center, Springfield, MA, USA; [17] ImmunoGen, Inc., Waltham, MA, USA; [18]Fondazione Policlinico Universitario A. Gemelli, IRCCS and Catholic University of Sacred Heart, Rome, Italy; [19]University Hospital Leuven Leuven Cancer Institute, Leuven, Belgium

ENGOT European Network of Gynaecological Oncological Trial groups

GOG FOUNDATION® Transforming the standard of care™

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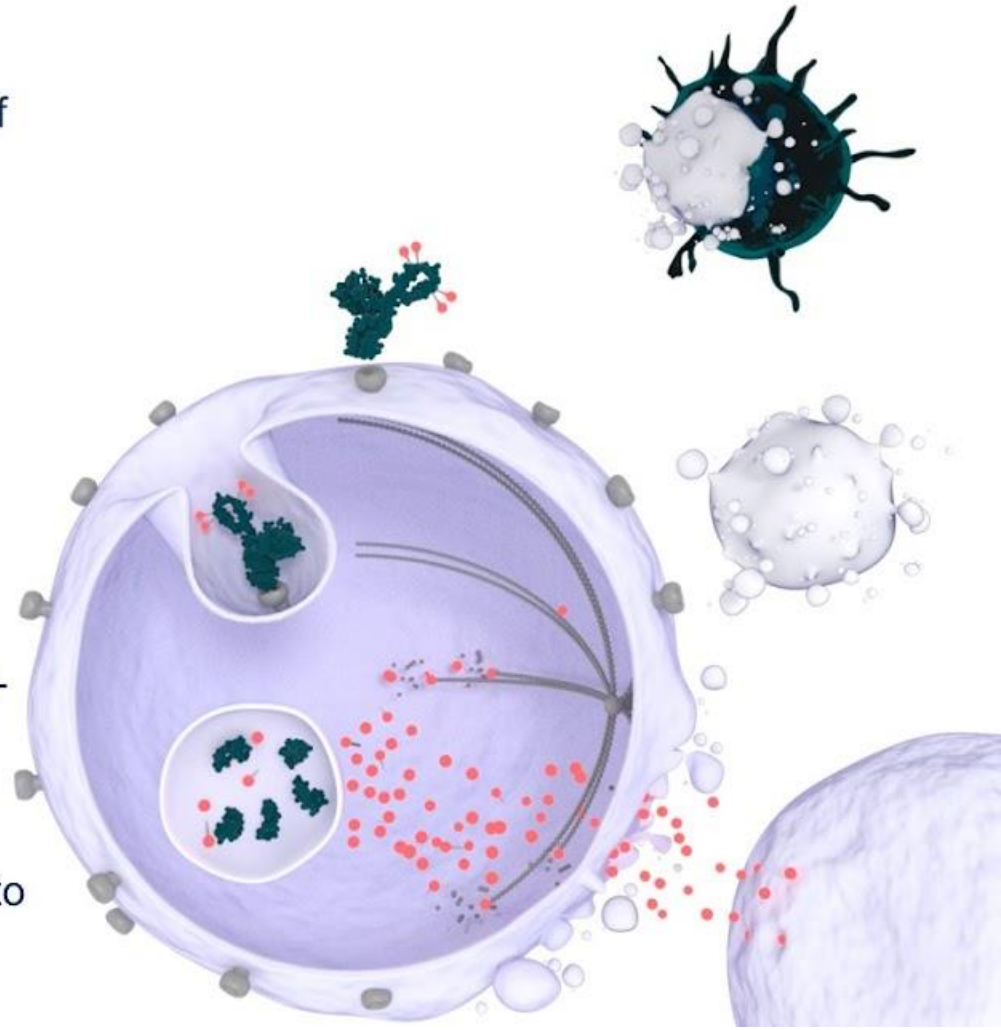
Background

- No randomized phase 3 trial has shown an overall survival (OS) benefit of a novel therapy in platinum-resistant ovarian cancer (PROC)[1, 2]
- Mirvetuximab soravtansine (MIRV) is an ADC comprising a FRα-binding antibody, cleavable linker, and maytansinoid DM4, a potent tubulin-targeting agent[3,4]
- FRα is expressed in ~90% of ovarian carcinomas,[5, 6] with 35-40%[7] of PROC tumors exhibiting high FRα expression (≥75% of tumor cells positive with ≥2+ intensity)[8]
- MIRV demonstrated an ORR of 32% and mDOR 6.9 months in the single-arm study SORAYA[8] of BEV pre-treated PROC to support accelerated approval by the FDA[9]
- MIRASOL is the confirmatory, randomized, global phase 3 trial designed to support approval worldwide



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MIRASOL (NCT04209855) – Study Design[1,2]

An open-label, phase 3 randomized trial of MIRV vs investigator's choice chemotherapy in patients with FRα-high platinum-resistant ovarian cancer

Patient Population
(N=453)

Enrollment and Key Eligibility

Platinum-resistant disease (PFI ≤6 mo)

FRα detected by IHC with PS2+ intensity among ≥75% of viable tumor cells

High-grade serous histology

1º platinum-refractory disease excluded (primary PFI <3 mo)

1-3 prior lines of therapy

Prior BEV and PARPi allowed

Patients with BRCA mutations allowed

1:1 Randomization

Treatment Regimen-Experimental

MIRV
(6 mg/kg AIBW Q3W)

Treatment Regimen-Control

Investigator's Choice Chemotherapy
(Paclitaxel, PLD, or Topotecan)

Stratification Factors

IC chemo: paclitaxel, PLD, or topotecan

Prior lines of therapy: 1 vs 2 vs 3

Primary Endpoint

PFS by INV
(BICR sensitivity analysis)

Key Secondary Endpoints

1) ORR by INV
2) OS
3) PROs[a]

Secondary Endpoints

Safety and tolerability
DOR
CA-125 response[b]
PFS2

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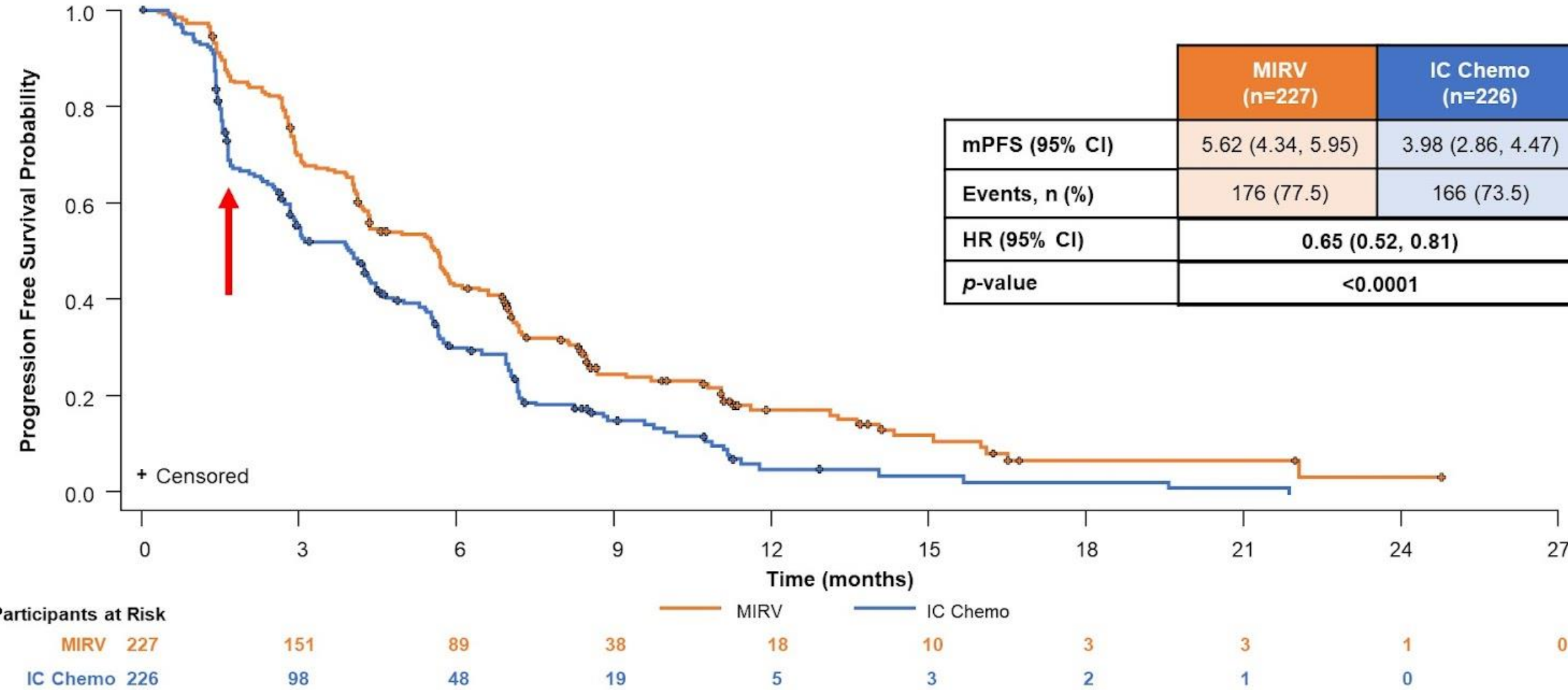
Primary Endpoint: Progression-Free Survival by Investigator



	MIRV (n=227)	IC Chemo (n=226)
mPFS (95% CI)	5.62 (4.34, 5.95)	3.98 (2.86, 4.47)
Events, n (%)	176 (77.5)	166 (73.5)
HR (95% CI)	0.65 (0.52, 0.81)	
p-value	<0.0001	

No. Participants at Risk									
MIRV	227	151	89	38	18	10	3	3	1	0
IC Chemo	226	98	48	19	5	3	2	1	0	

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Overall Response Rate by Investigator (N=453)

	MIRV (n=227)	IC Chemo (n=226)
ORR **n, 95% CI**	**42%** 96, (35.8, 49.0)	**16%** 36, (11.4, 21.4)
Best overall response, n (%)		
CR	12 (5%)	0
PR	84 (37%)	36 (16%)
SD	86 (38%)	91 (40%)
PD	31 (14%)	62 (27%)
Not evaluable	14 (6%)	37 (16%)

ORR Difference 26.4% (18.4, 34.4)
OR 3.81 (2.44, 5.94)
***p*<0.0001**

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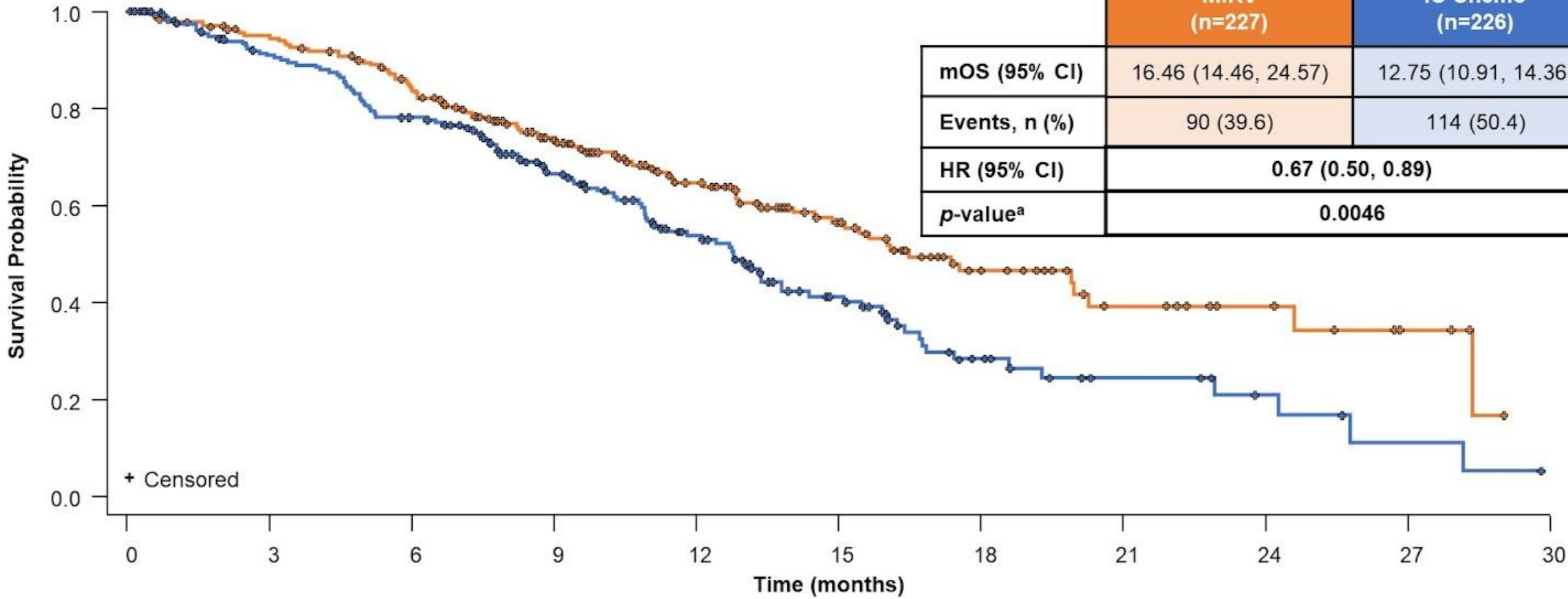
Overall Survival

	MIRV (n=227)	IC Chemo (n=226)
mOS (95% CI)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)
Events, n (%)	90 (39.6)	114 (50.4)
HR (95% CI)	0.67 (0.50, 0.89)	
p-value[a]	0.0046	



No. Participants at Risk

MIRV	227	204	175	128	82	53	28	15	9	4	0
IC Chemo	226	185	157	107	68	39	18	9	5	2	0

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Progression-Free and Overall Survival in Bevacizumab-Naïve and Prior Bevacizumab-Treated Subsets by Investigator

	Bev-Naïve		Prior Bev	
	MIRV	IC Chemo	MIRV	IC Chemo
mPFS (95% CI)	7.0 (5.6, 8.4)	5.6 (3.0, 6.5)	4.4 (4.0, 5.8)	3.0 (2.5, 4.3)
Events n (%)[a]	65 (73.0)	57 (69.0)	111 (80.4)	109 (76.2)
HR (95% CI)	**0.66 (0.46, 0.94)**		**0.64 (0.49, 0.84)**	
Nominal *p*-value	0.0210		0.0011	
mOS (95% CI)	20.2 (14.8, NE)	14.4 (11.8, 16.7)	15.4 (11.3, 17.5)	10.9 (9.4, 13.3)
Events n (%)[a]	23 (25.8)	39 (47.0)	67 (48.6)	75 (52.4)
HR (95% CI)	**0.51 (0.31, 0.86)**		**0.74 (0.54, 1.04)**	
Nominal *p*-value	0.0099		0.0789	

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Safety Summary (N=425)

MIRV has a tolerable safety profile compared with IC Chemo

	MIRV (n=218)	IC Chemo (n=207)
Any TEAE, n (%)	210 (96)	194 (94)
Grade 3+ TEAEs, n (%)	91 (42)	112 (54)
SAEs, n (%)	52 (24)	68 (33)
Deaths on study drug or within 30 days of last dose, n (%)	5 (2)	5 (2)
Dose reductions due to TEAEs, n (%)	74 (34)	50 (24)
Dose delays due to TEAEs, n (%)	117 (54)	111 (54)
Discontinuations due to TEAEs, n (%)	20 (9)	33 (16)

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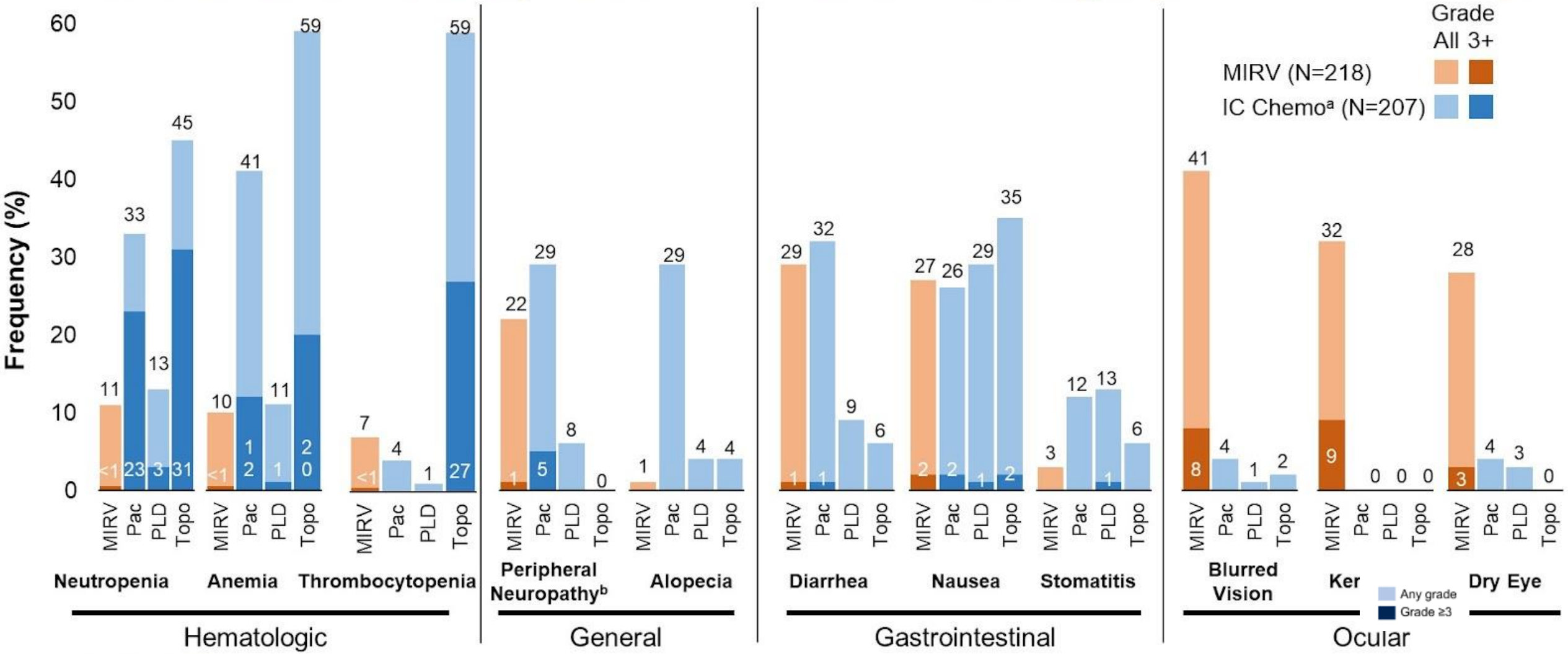
Differentiated Safety Profile: Treatment-Emergent Adverse Events



Endometrial cancer

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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

Eligible patients

- Histologically/cytologically proven advanced or recurrent EC
- Stage III/IV disease or first recurrent EC with low potential for cure by radiation therapy or surgery alone or in combination
  - Carcinosarcoma, clear cell, serous, or mixed histology permitted[a]
- Naïve to systemic therapy or systemic anticancer therapy and had a recurrence or PD ≥6 months after completing treatment
- ECOG PS 0-1
- Adequate organ function

Stratification

- MMR/MSI status[b]
- Prior external pelvic radiotherapy
- Disease status

R1:1

Dostarlimab IV 500 mg
Carboplatin AUC 5 mg/mL/min
Paclitaxel 175 mg/m^2 Q3W for 6 cycles

Dostarlimab IV 1000 mg Q6W up to 3 years[c]

Placebo
Carboplatin AUC 5 mg/mL/min
Paclitaxel 175 mg/m^2 Q3W for 6 cycles

Placebo IV Q6W up to 3 years[c]

Follow-up

Primary endpoint

- PFS by INV per RECIST v1.1
- OS

Secondary endpoints

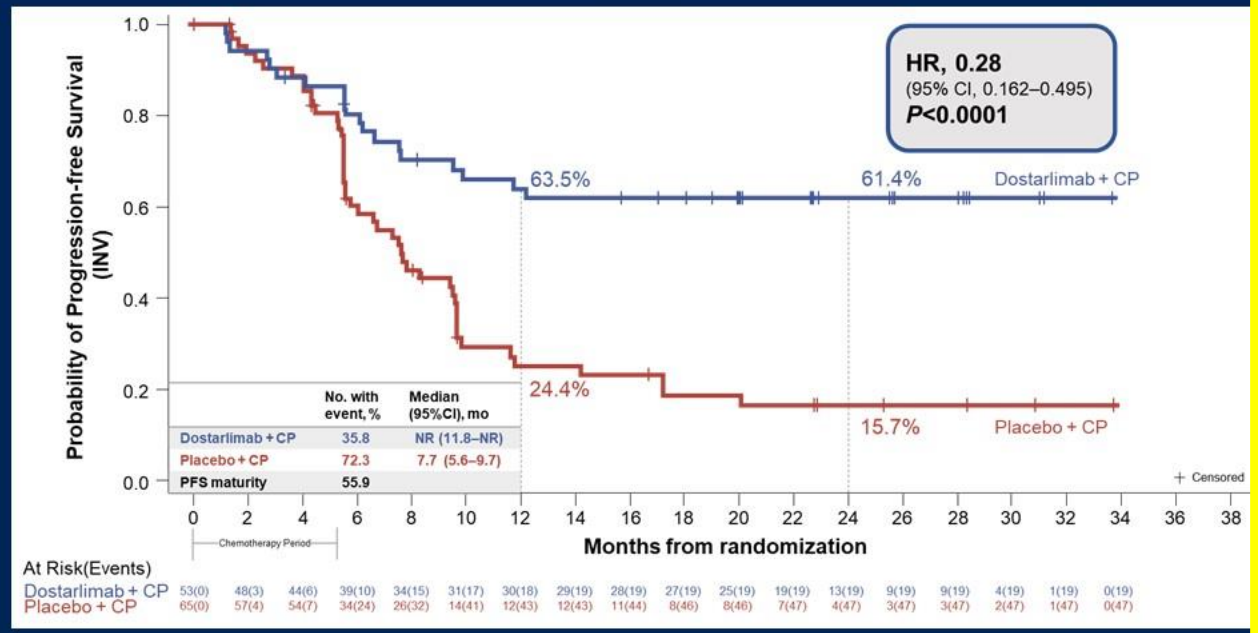
- PFS by BICR
- PFS2
- ORR
- DOR
- DCR
- HRQOL/PRO
- Safety

N=494
118/494 (23.8%) dMMR/MSI-H
≃ 80% without previous pelvic radiation
≃ 50% recurrent

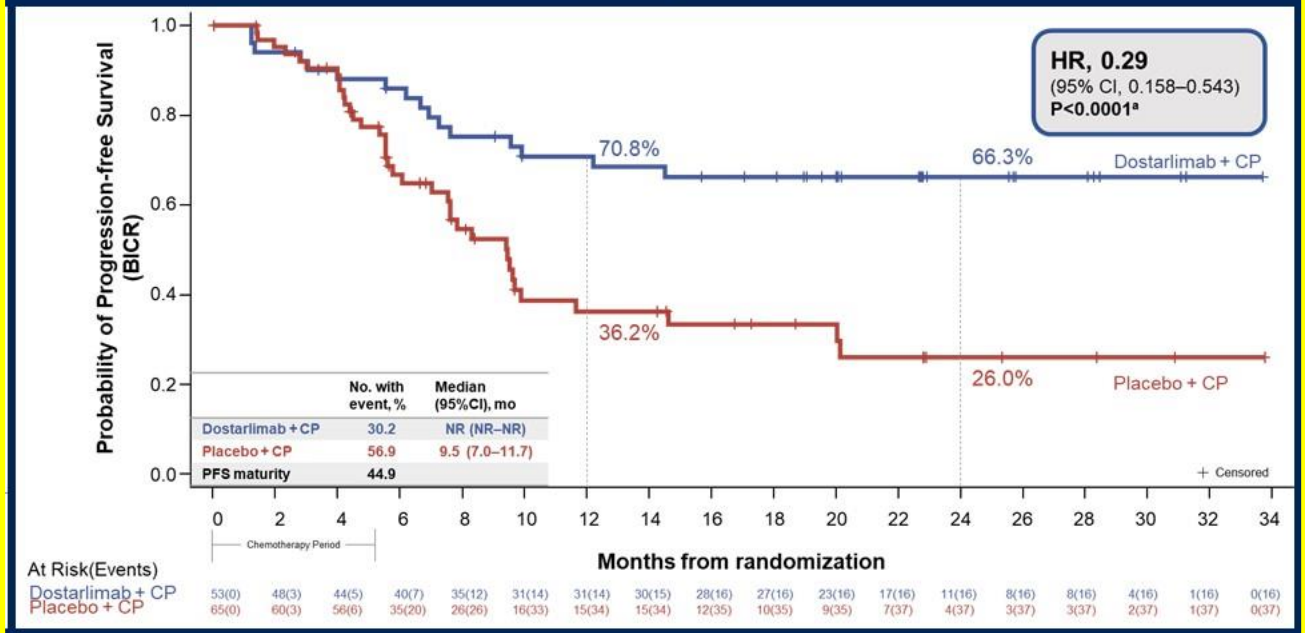
PFS by INV and by BICR Consistent in dMMR/MSI-H Population

118 pts/494 (23.8%)

INV



BICR



Agreement on occurence:

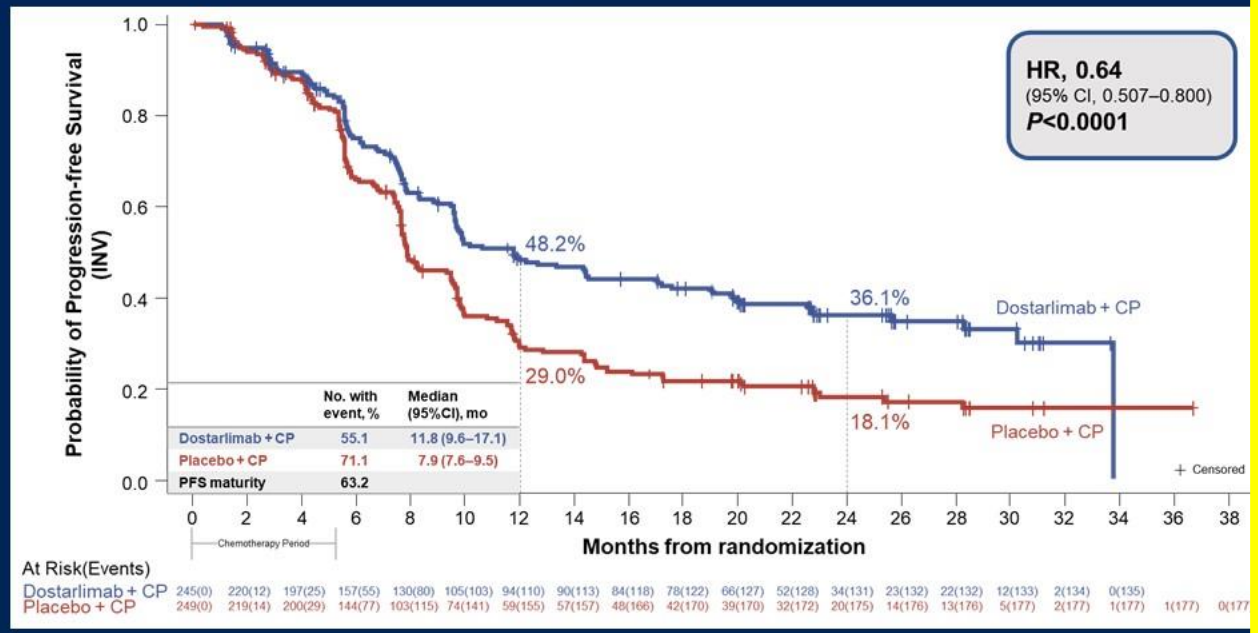
Dostarlimab + CP group 83%

Placebo + CP group 78.5%

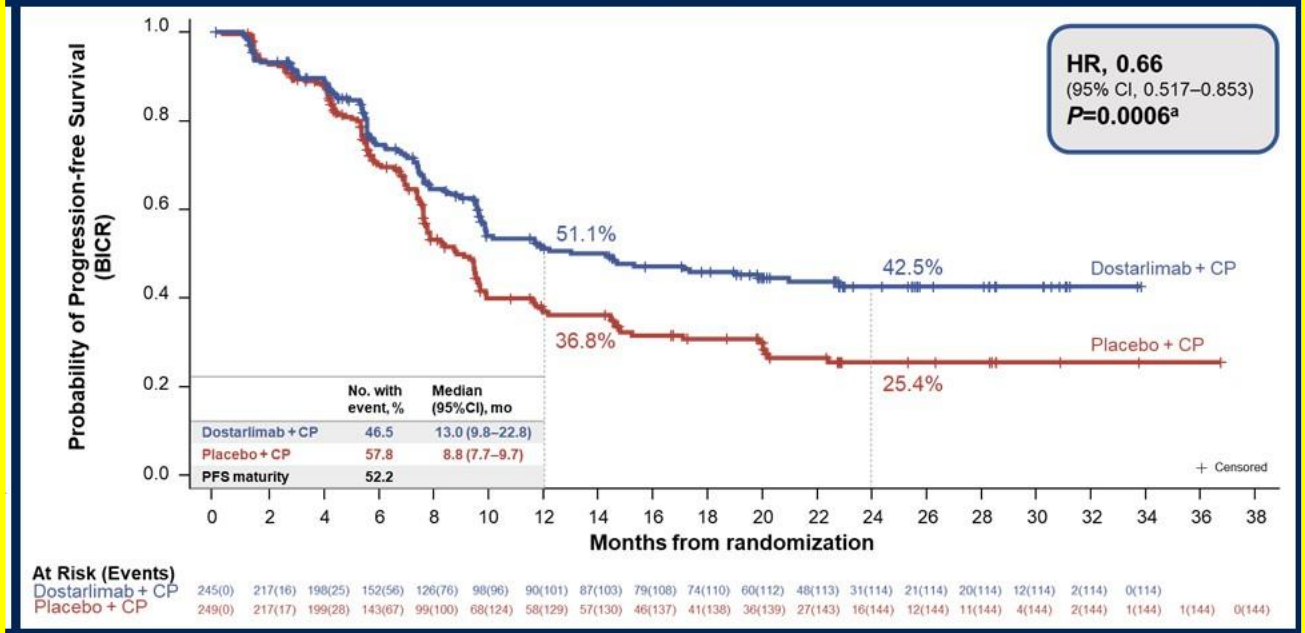
Median duration of follow-up: 24.79%

PFS by INV and by BICR Consistent in Overall Population

INV



BICR

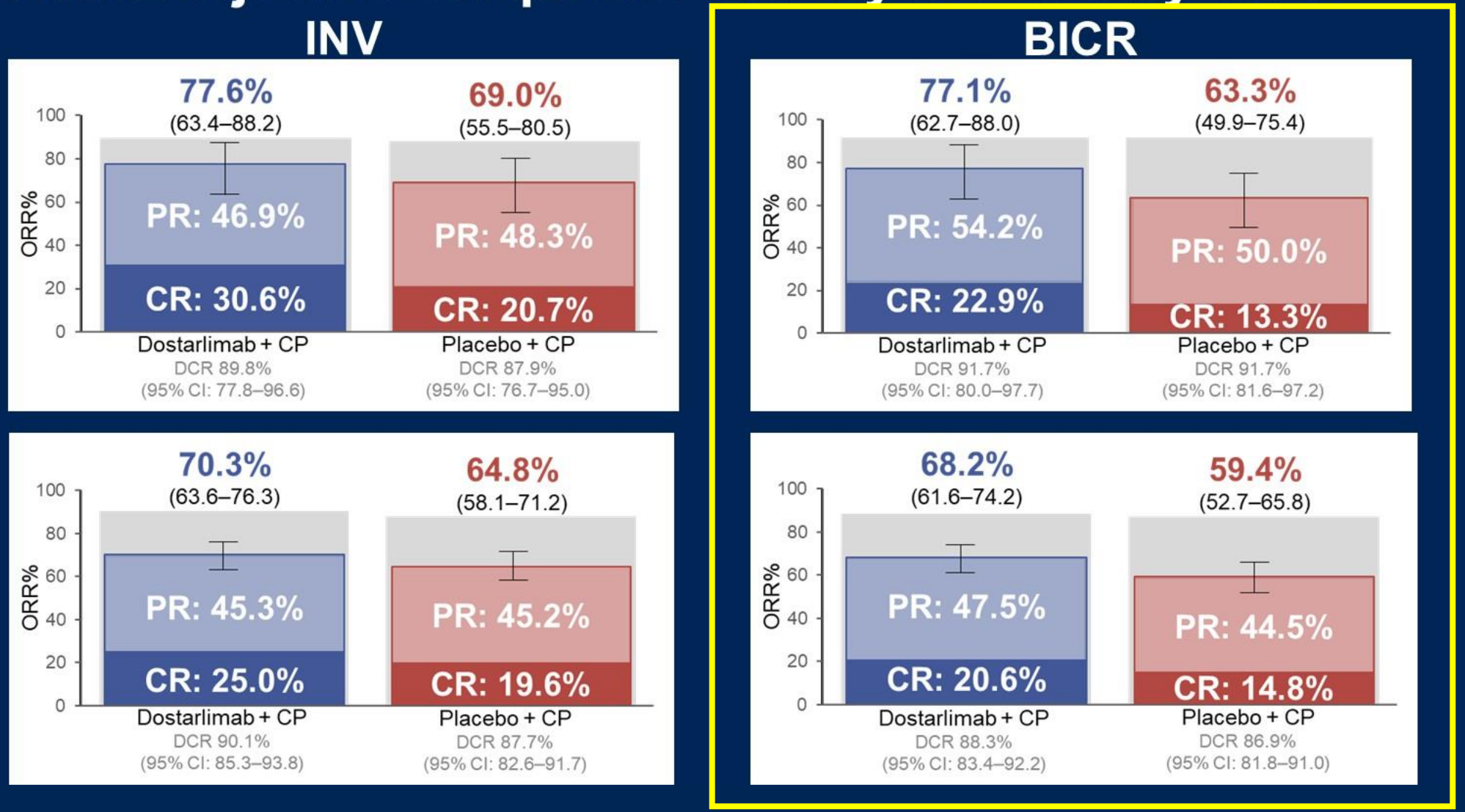


Agreement on occurence:

Dostarlimab + CP group 83.3%

Placebo + CP group 81.2%

Consistent Objective Response Rate by INV and by BICR[a]



Safety Summary

Parameter, n (%)	Dostarlimab + CP (N=241)	Placebo + CP (N=246)
Any TEAE	241 (100)	246 (100)
Any grade ≥3 TEAE	170 (70.5)	147 (59.8)
Serious TEAE	91 (37.8)	68 (27.6)
Any treatment-related irAE	92 (38.2)	38 (15.4)
Any TEAE leading to discontinuation of dostarlimab or placebo	42 (17.4)	23 (9.3)
Any TEAE leading to discontinuation of carboplatin	24 (10.0)	19 (7.7)
Any TEAE leading to discontinuation of paclitaxel	24 (10.0)	23 (9.3)
Any TEAE leading to death	5 (2.1)[a]	0
Any TEAE related to dostarlimab leading to death	2 (0.8)[b]	—
Median duration of overall treatment (range), weeks	43.0 (3.0–150.9)	36.0 (2.1–165.1)

[a]3 deaths were not related to study treatment (opiate overdose, COVID-19, and general physical health deterioration). [b]One death was considered by the investigator as related to dostarlimab plus CP and occurred during the first 6 cycles (myelosuppression); one death was related to dostarlimab and occurred during the 90-day safety follow-up (hypovolemic shock).
CP, carboplatin/paclitaxel; irAE, immune-related adverse event; TEAE, treatment-emergent adverse event.

PRO Assessments

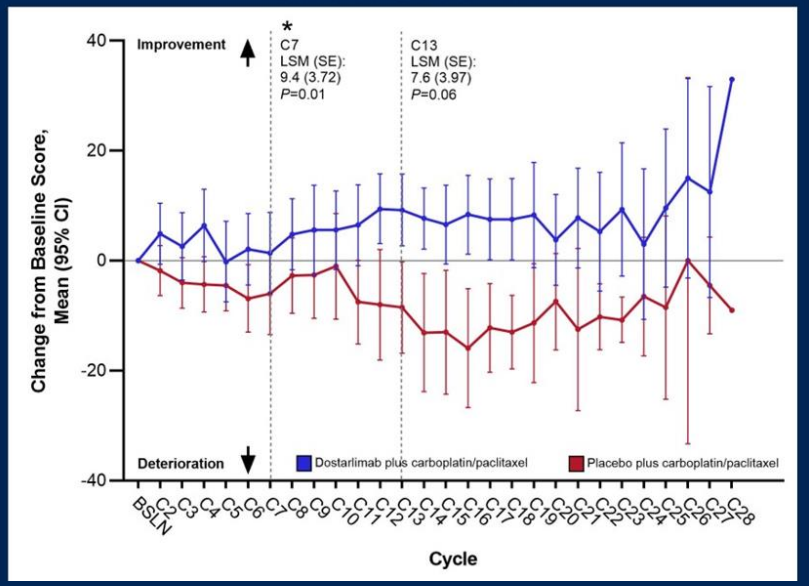
EORTC QLQ-C30 And QLQ-EN24

Significant difference **at C7 (end of chemo phase)** in global QoL between arms in **dMMR/MSI-H population**

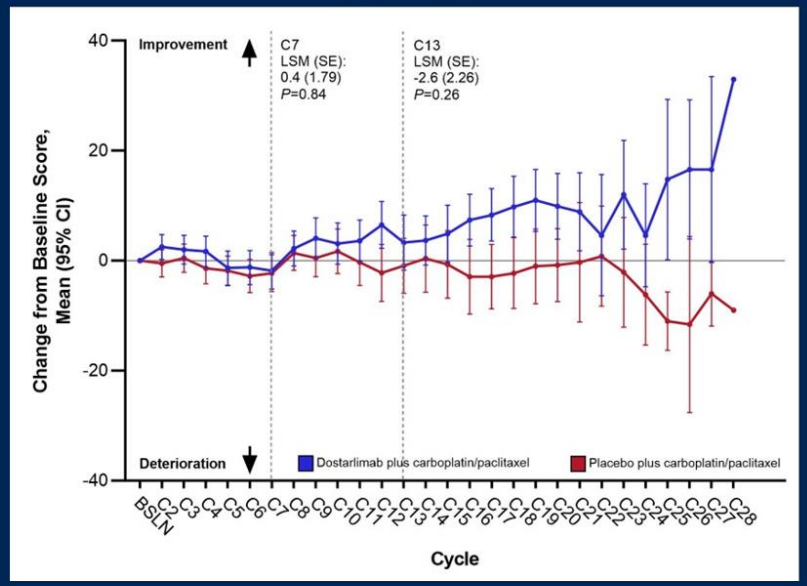
Dostarlimab: no detrimental effects on QoL

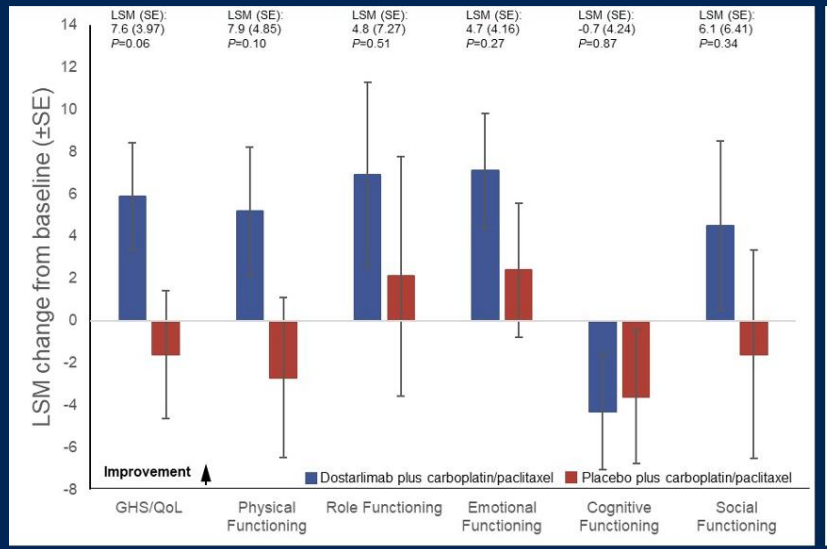
No significant differences **at C13 (start of 2ndyear of treatment)**

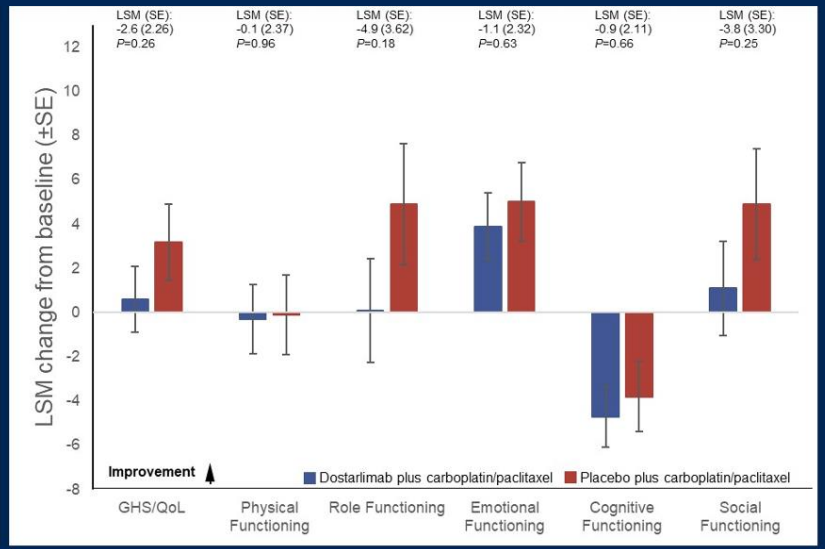
dMMR/MSI-H



Overall







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2023 ASCO® ANNUAL MEETING

Camrelizumab plus apatinib in patients with advanced or recurrent endometrial cancer after failure of at least one prior systemic therapy (CAP 04): A single-arm phase II trial

Huaying Wang[1,2*], Wenjuan Tian[1,2], Yulan Ren[1,2], Jing Lu[2,3], Tingting Wang[4,5], Haiming Li[2,3], Chuyu Jing[1,2], Boer Shan[1,2], Huijuan Yang[1,2], Xi Cheng[1,2]

1. Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center, Shanghai, China
2. Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China
3. Department of Radiology, Fudan University Shanghai Cancer Center, Shanghai, China
4. Department of Nuclear Medicine, Institute of Clinical Nuclear Medicine, Renji Hospital;
5. School of Medicine, Shanghai Jiao Tong University, Shanghai, China

* Corresponding author

Study Design

- **This is a single-arm, Simon's two-stage designed phase II study.**

Patients

- Confirmed advanced recurrent or metastatic endometrial cancer
- Progressed on or after at least one prior systemic therapy
- ECOG PS 0-1
- Immunotherapy naïve

N=36

Treatment

Camrelizumab 200mg, iv, Q2W, up to 2 year

Apatinib 250mg, po, QD

Until disease progression, intolerable toxicity.

Primary endpoint

- Objective response rate (ORR) by RECIST 1.1

Secondary endpoints

- Disease control rate (DCR)
- Duration of response (DoR)
- Time to response (TTR)
- Progression-free survival (PFS)
- Overall survival (OS)
- Safety

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Patients

	Patients (n = 36)
Age, years	
Median (range)	60 (29,76)
<65 years, n(%)	23 (63.9)
65 years, n(%)	13 (36.1)
ECOG performance status, n (%)	
0	19 (52.8)
1	17 (47.2)
Histologic features, n (%)	
Endometrioid adenocarcinoma	28 (77.8)
FIGO grade 1	4 (11.1)
FIGO grade 2	12 (33.3)
FIGO grade 3	11 (30.6)
Unknown	1 (2.8)
Serous carcinoma	6 (16.7)
Mixed	1 (2.8)
Endometrial clear cell carcinoma	1 (2.8)

	Patients (n = 36)
FIGO stage*, n (%)	
I-II	14 (38.9)
III-IV	22 (61.1)
Prior treatment lines, n (%)	
1	21 (58.3)
2	7 (19.4)
≥3	8 (22.2)
Prior therapy, n (%)	
Radiotherapy	19 (52.8)
Anti-angiogenic therapy	10 (27.8)
Microsatellite status, n(%)	
MSI-H/dMMR	2 (5.6)
MSS/pMMR	25 (69.4)
Unknown	9 (25.0)
PD-L1 status, n(%)	
Positive	7 (19.4)
Negative	17 (47.2)
Unknown	12 (33.3)

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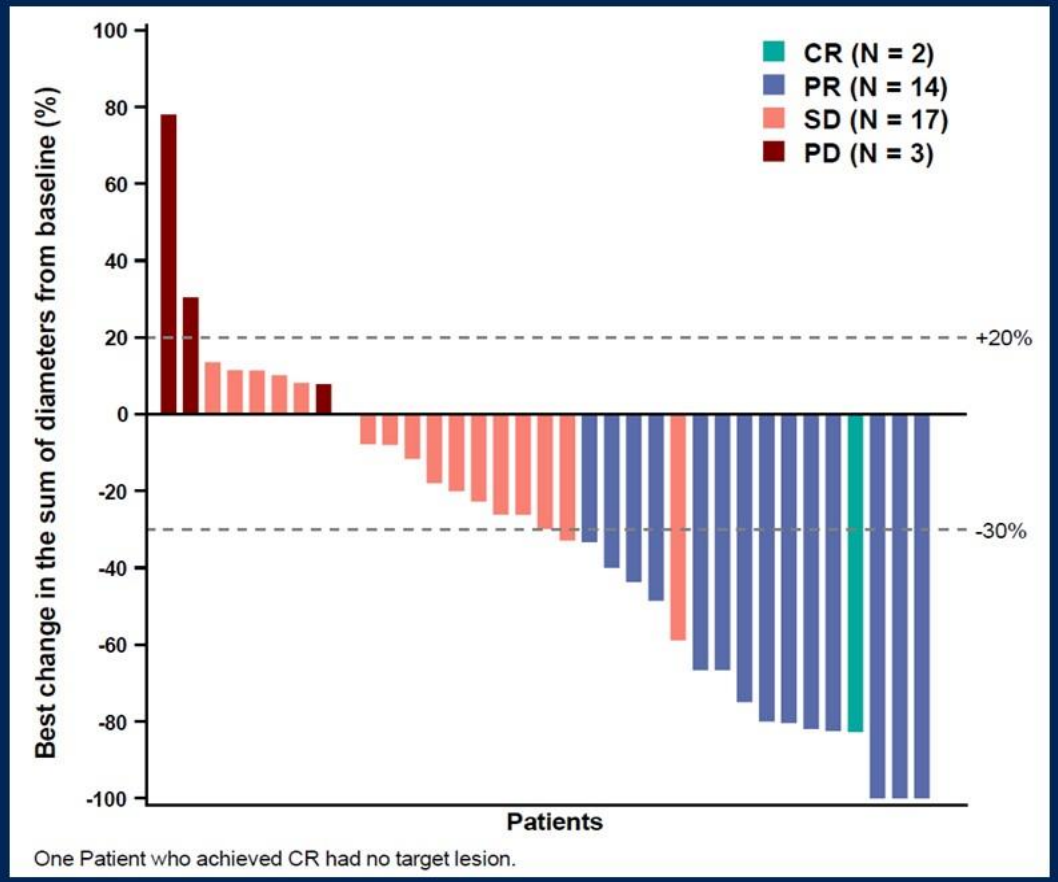
Confirmed Overall Response

Median follow-up: 14 months

	Patients (n=36)
Confirmed ORR*, % (95% CI)	44.4 (27.9,61.9)
Confirmed DCR, % (95% CI)	91.7 (77.5,98.2)
Confirmed response, n (%)	
CR	2# (5.6)
PR	14 (38.9)
SD	17 (47.2)
PD	3 (8.3)
Median DOR (95% CI), mo	9.9 (4.2, NR)
DoR≥6 months, n(%)	9 (25.0%)
DoR≥12 months, n(%)	4 (11.1%)



*16 responders in the first 34 patients with an ORR of 47.1%, the study was considered positive.
#1 patient had no target lesion but one non-target lesion, overall response met CR criteria of RECIST1.1 after treatment.

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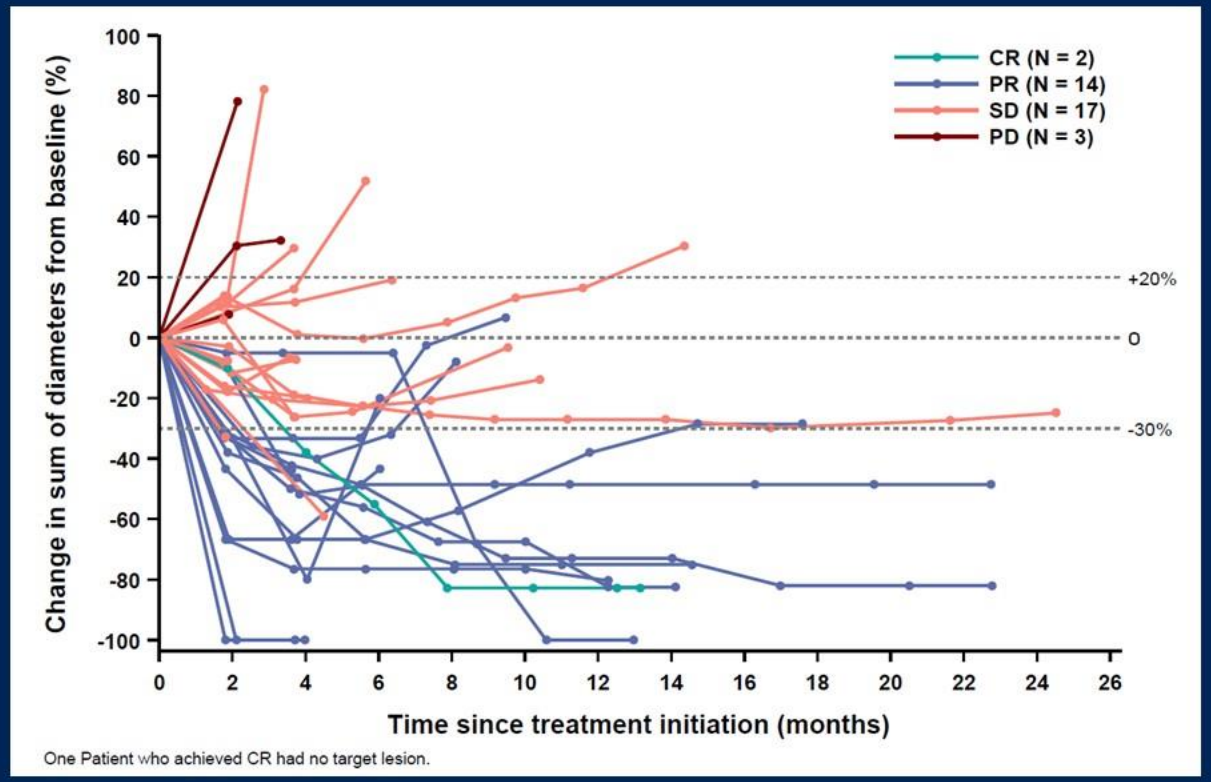
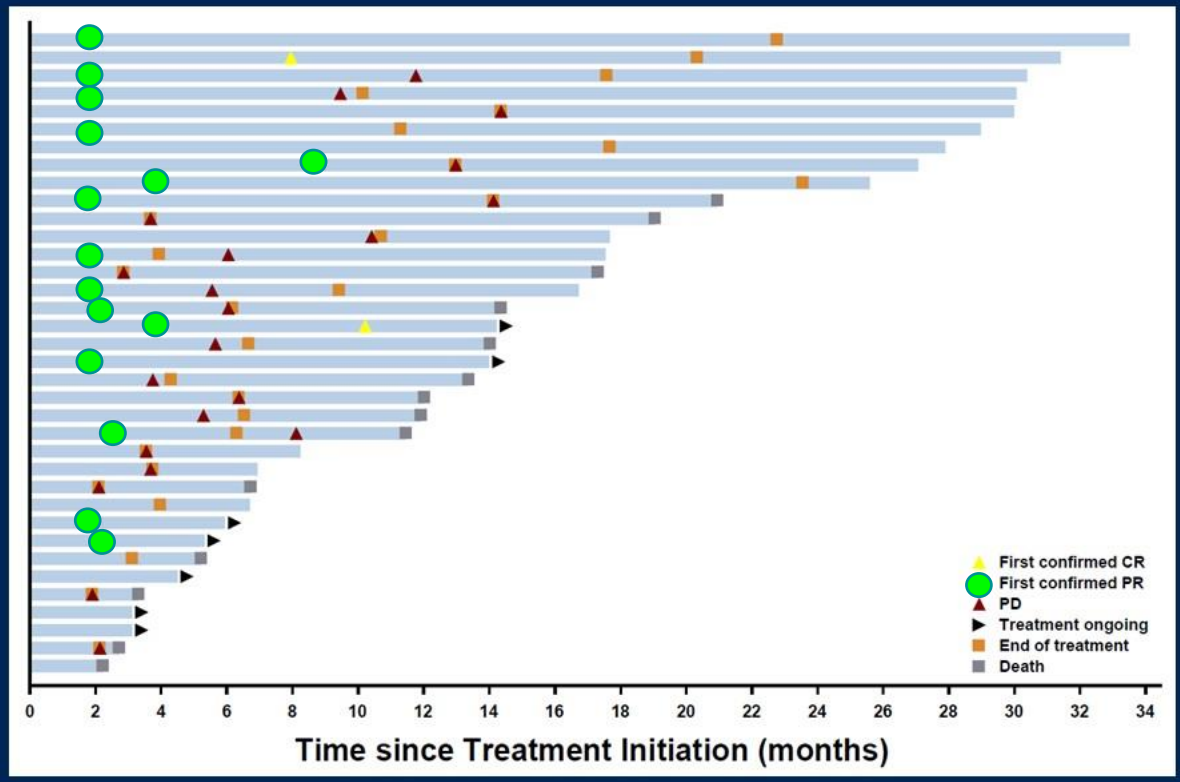
Objective Responses and Treatment Duration

- Median TTR was 1.9 months (95% CI: 1.8, 2.5)
- 13 (36.1%) of 36 patients had response at the first radiographical assessment



One Patient who achieved CR had no target lesion.



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Common TRAEs

	Number of patients (N =36)		
	Any grade	Grade 1-2	Grade 3-4
Any adverse events	33 (91.7)	17 (47.2)	16 (44.4)
Alanine aminotransferase increased	16 (44.4)	12 (33.3)	4 (11.1)
Hypertension	15 (41.7)	11 (30.6)	4 (11.1)
Y-glutamyl transferase increased	13 (36.1)	6 (16.7)	7 (19.4)
Aspartate aminotransferase increased	13 (36.1)	9 (25.0)	4 (11.1)
Palmar-plantar erythrodysesthesia syndrome	11 (30.6)	11 (30.6)	0
Neutrophil count decreased	9 (25.0)	9 (25.0)	0
White blood cell count decreased	9 (25.0)	8 (22.2)	1 (2.8)
Proteinuria	9 (25.0)	8 (22.2)	1 (2.8)
Hypothyroidism	8 (22.2)	6 (16.7)	2 (5.6)
Platelet count decreased	7 (19.4)	7 (19.4)	0
Reactive cutaneous capillary endothelial proliferation	6 (16.7)	6 (16.7)	0
Blood bilirubin increased	6 (16.7)	4 (11.1)	2 (5.6)

2 (5.6%) treatment withdrawal due to AE

Potential irAEs

	Number of patients (N =36)		
	Any grade	Grade 1-2	Grade 3-4
Any adverse events	19 (52.8)	8 (22.2)	11 (30.6)
Alanine aminotransferase increased	8 (22.2)	4 (11.1)	4 (11.1)
Aspartate aminotransferase increased	8 (22.2)	4 (11.1)	4 (11.1)
Hypothyroidism	8 (22.2)	6 (16.7)	2 (5.6)
Reactive cutaneous capillary endothelial proliferation	6 (16.7)	6 (16.7)	0
Y-glutamyl transferase increased	4 (11.1)	0	4 (11.1)
Creatine phosphokinase increased	4 (11.1)	4 (11.1)	0
Blood bilirubin increased	3 (8.3)	1 (2.8)	2 (5.6)
Hyperglycemia	3 (8.3)	0	3 (8.3)
Platelet count decreased	2 (5.6)	2 (5.6)	0
Hyperthyroidism	1 (2.8)	0	1 (2.8)

No treatment-related deaths

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Cervical cancer

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GCIG GYNECOLOGIC CANCER INTERGROUP

Canadian Cancer Trials Group | Groupe canadien des essais sur le cancer

An international randomized phase III trial comparing radical hysterectomy and pelvic node dissection vs simple hysterectomy and pelvic node dissection in patients with low-risk early-stage cervical cancer

A Gynecologic Cancer Intergroup study led by the Canadian Cancer Trials Group

CCTG CX.5 - SHAPE

NCT01658930

Marie Plante, Janice Kwon, Sarah Ferguson, Vanessa Samouelian, Gwenael Ferron, Amandine Maulard, Cor de Kroon, Willemien Van Driel, John Tidy, Sven Mahner, Stefan Kommoss, Frederic Goffin, Christian Marth, Karl Tamussino, Brynhildur Eyjolfsdottir, Jae-Weon Kim, Noreen Gleeson, Juliana Ubi, Lori Brotto, Dongsheng Tu, Lois Shepherd

On behalf of the SHAPE investigators

Trial Schema

Low-risk cervical cancer as defined by:

- Squamous cell, adenocarcinoma, adenosquamous carcinoma
- Stage IA2 and IB1
- < 10 mm stromal invasion on LEEP/cone
- < 50% stromal invasion on MRI
- Max dimension of ≤ 20 mm
- Grade 1-3 or not assessable

Stratification:

1. **Cooperative Group**
2. **Sentinel node mapping** (Yes vs No)
3. **Stage** (IA2 vs IB1)
4. **Histological type** (Squamous vs adenocarcinoma/adenosquamous)
5. **Grade** (1-2 vs 3 vs not assessable)

RANDOMIZE 1:1

Arm 1 (Control)
Radical Hysterectomy*

Arm 2 (Experimental)
Simple Hysterectomy*

Primary endpoint

Pelvic recurrence rate at 3 years

Secondary endpoints:

- RFS
- Pelvic RFS *
- Extrapelvic RFS
- OS
- PROs
- Rate of SN detection, positive PLN, parametrial involvement, involved surgical margins

*Regardless of treatment assignment, surgery will include **pelvic lymph node dissection** with optional sentinel lymph node (SN) mapping. If SN mapping is to be done, the mode is optional, but the laparoscopic approach is preferred.

*Primary endpoint in original design (Amendment in jun 22 due to very low event rate)

Statistical Considerations

- **Non-inferiority Phase 3 design**
- ITT analysis as primary analysis; per protocol analysis as secondary analysis
- PRR3 was estimated using Kaplan-Meier method
- **Non-inferiority of SH to RH is claimed when the upper 1-sided 95% confidence limit for the difference in PRR3 for SH to RH is lower than or equal to 4%**
- With **700 patients randomized** and **followed for a minimum of 3 years**, the study has **85% power to claim non-inferiority of SH to RH** when PRR3 in both arms are assumed to be same

Sample size calculation for non-inferiority trials

Power	Non-Inferiority Margin	Sample Size
85%	1%	**11,042**
85%	2%	**2,760**
85%	3%	**1,226**
85%	4%	**700**

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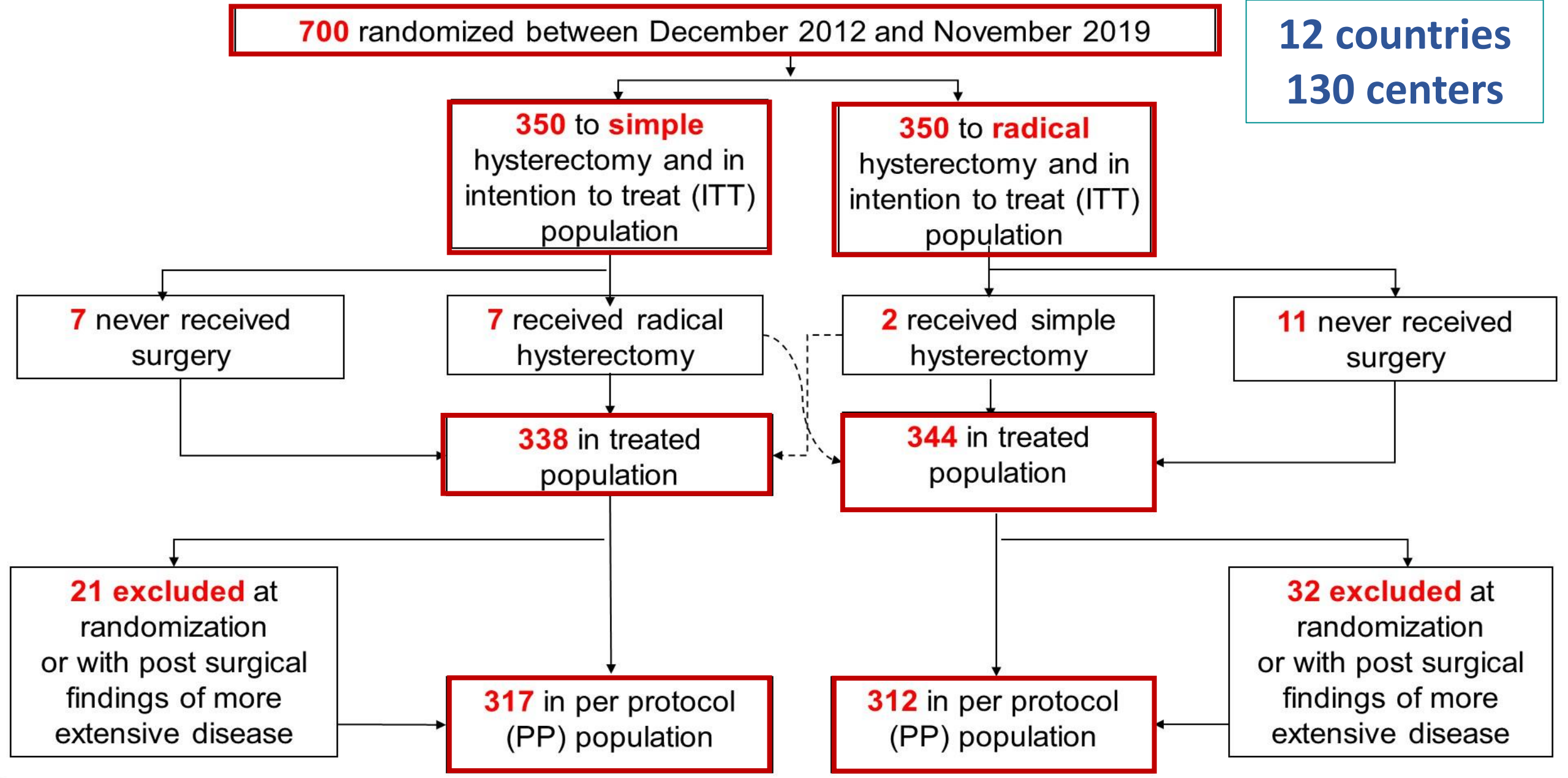

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Key Baseline Patient Characteristics

Characteristics	Simple Hysterectomy N=350 (%)	Radical Hysterectomy N=350 (%)	Total N=700
Age (years): Median (range)	42 (26-77)	45 (24-80)	44 (24-80)
• ≤ 50 years old (%)	271 (77.4)	246 (70.3)	517 (73.9)
ECOG status: 0	336 (96)	335 (95.7)	671 (95.9)
BMI: median (range)	25 (16.4-53.3)	24.8 (16.1-52)	24.8 (16.1-57.6)
Diagnostic Procedure			
• LEEP / Cone	254 (72.6)	226 (64.6)	480 (68.6)
• Cervical Biopsy	52 (14.9)	77 (22)	129 (18.4)
• Both	40 (11.4)	41 (11.7)	81 (11.6)
• Missing	4 (1.1)	6 (1.7)	10 (1.4)
FIGO Stage:			
• IA2	30 (8.6)	28 (8.0)	58 (8.3)
• IB1	320 (91.4)	322 (92.0)	642 (91.7)
Histology			
• Squamous	218 (62.3)	214 (61.1)	432 (61.7)
• Adenocarcinoma	114 (32.6)	131(37.4)	245 (35.0)
• Adenosquamous	18 (5.1)	5 (1.4)	23 (3.3)
Grade:			
• 1 or 2	205 (58.6)	210 (60.0)	415 (58.2)
• 3	49 (14)	49 (14)	98 (14)
• Not assessed	96 (27.4)	91 (26)	187 (26.7)

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All Treated Patients Post Surgery

Characteristics	Simple Hysterectomy N=338 (%)	Radical Hysterectomy N=344 (%)	P-value
Type of Surgical Approach *			
• Abdominal	57 (16.9)	99 (28.8)	**0.0003**
• Laparoscopic	188 (55.6)	152 (44.2)	**0.0036**
• Robotic	82 (24.3)	87 (25.3)	0.79
• Vaginal	11 (3.3)	4 (1.2)	0.07
Sentinel Node Mapping			
• Planned	126 (37.3)	131 (38.2)	0.87
• Successful	78/126 (61.9)	83/131 (63.4)	0.90

* Surgical approach: at the discretion of the surgeon; not a randomization factor

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All Treated Patients Post Surgery

Key post surgical findings on final pathology	Simple hysterectomy N=338 (%)	Radical hysterectomy N=344 (%)	P-value
• **Residual cervical cancer detected**	154 (45.6)	163 (47.4)	0.65
• **Lymphovascular space invasion (LVSI)**	45 (13.3)	45 (13.1)	1.00
• **Positive nodes** (from sentinel or non sentinel nodes)	11 (3.3)	15 (4.4)	0.55
• **Positive vaginal margins**	7 (2.1)	10 (2.9)	0.62
• **Positive parametrium**	0	6 (1.7)	0.03
• **Lesions > 2cm**	15 (4.4)	14 (4.1)	0.85

Adjuvant Treatment	Simple hysterectomy N=338 (%)	Radical hysterectomy N=344 (%)	P-value
• **Adjuvant Post Operative Treatment**	31 (9.2)	29 (8.4)	0.79
• Chemotherapy only	1	0	
• Radiation therapy only	15	11	
• Chemoradiation	15	18	

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Recurrences

Events	Simple Hysterectomy N=350 (%)	Radical Hysterectomy N=350 (%)	Total N=700 (%)
Pelvic recurrences	11 (3.1)	10 (2.9)	21 (3.0)
• Vaginal Vault	9 (0.4)	8 (2.3)	17 (2.4)
• Parametrium	1 (0.3)	0	1 (0.1)
• Pelvic Lymph Nodes	0	0	0
• Other	1 (0.3)	2 (0.6)	3 (0.4)
Extra Pelvic recurrences	7 (2.0)	2 (0.6)	9 (1.3)
• Abdomen	2 (0.6)	0	2 (0.3)
• Para-aortic lymph nodes	2 (0.6)	2 (0.6)	4 (0.6)
• Supraclavicular L N	1 (0.3)	0	1 (0.1)
• Other	2 (0.6)	0	2 (0.3)
Pelvic and extra pelvic recurrences	3 (0.9)	2 (0.6)	5 (0.7)
Extra pelvic only recurrences	4 (1.1)	0	4 (0.6)
Pelvic or extra pelvic recurrences	15 (4.3)	10 (2.9)	25 (3.6)

median follow-up: 4.5 years

Deaths

Events	Simple Hysterectomy N=350 (%)	Radical Hysterectomy N=350 (%)	Total N=700 (%)
Deaths	7 (2.0)	7 (2.0)	14 (2.0)
• Cervical Cancer	4 (1.1)	1 (0.3)	5 (0.7)
• Other primary malignancy	1 (0.3)	3 (0.9)	4 (0.6)
• Other medical condition	2 (0.6)	3 (0.9)	5 (0.7)

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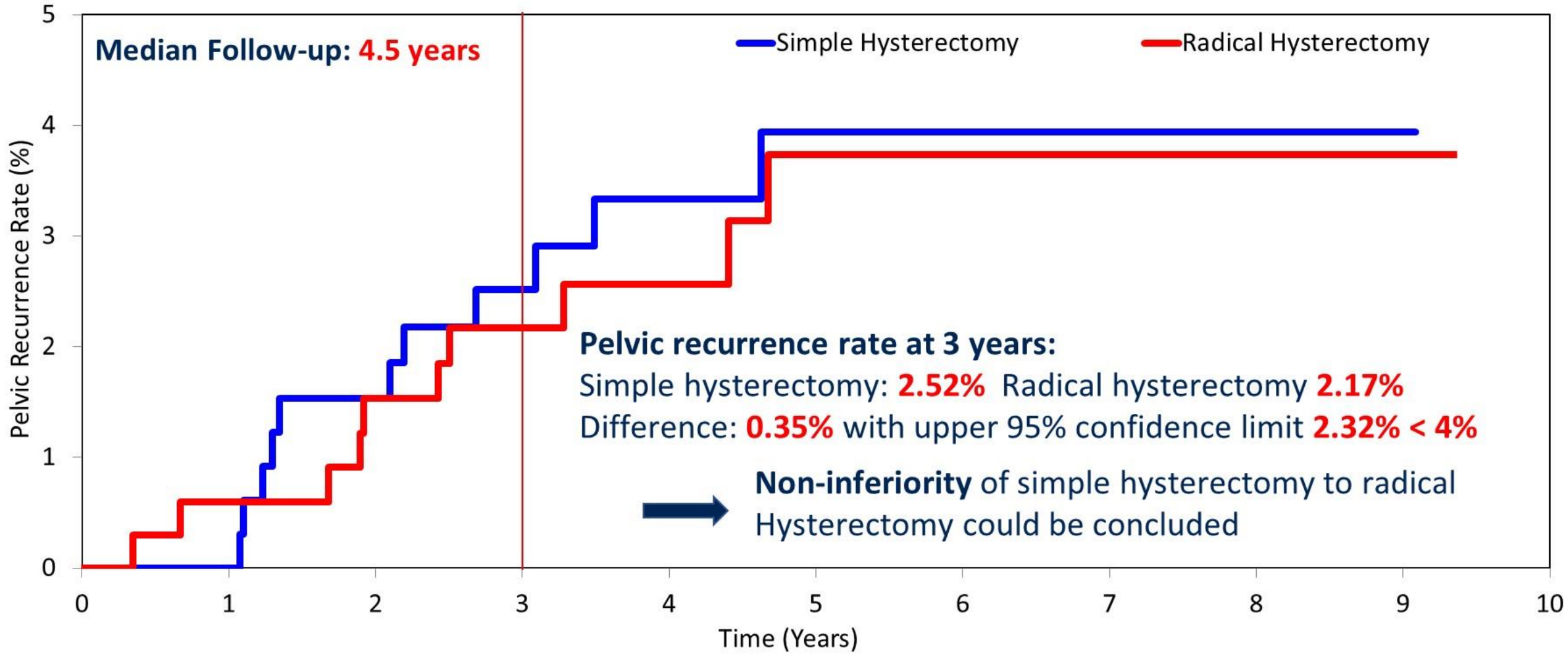
Pelvic Recurrence Rate (ITT)



Simple	350	328	311	273	204	133	61	31	14	4	0
Radical	350	329	315	286	208	132	66	31	16	2	0

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Secondary Efficacy Endpoints (ITT)

Endpoints	Simple Hysterectomy N=350	Radical Hysterectomy N=350		
	3 year outcomes		Hazard Ratio (90% confidence interval)	P-value
Pelvic Recurrence Free Survival	97.5%	97.8%	1.12 (0.54-2.32)	0.79
Extra-Pelvic Recurrence Free Survival	98.1%	99.7%	3.82 (0.79-18.4)	0.10
Relapse Free Survival	96.3%	97.8%	1.54 (0.69-3.45)	0.30
Overall Survival	99.1%	99.4%	1.09 (0.38-3.14)	0.87

Intraoperative complications	Simple Hysterectomy N=338 (%)	Radical Hysterectomy N=344 (%)	P-value
Intraoperative Injury	24 (7.1)	22 (6.4)	0.77
• Bladder	3	9	0.14
• Ureter	3	5	0.73
• Nerve	5	2	0.28
• Bowel	2	2	1.00
• Vein	4	1	0.21
• Other	7	3	0.22

Surgery-Related Adverse Events (All Grades with incidence ≥ 5% in one of the Arms)

Adverse Event	Simple Hysterectomy N=338 (%)	Radical Hysterectomy N=344 (%)	P value	Simple Hysterectomy N=338 (%)	Radical Hysterectomy N=344 (%)	P value
	Within 4 weeks of surgery (acute)			After 4 weeks of surgery (late)		
Any adverse event	144 (42.6)	174 (50.6)	**0.04**	181 (53.6)	208 (60.5)	**0.08**
• Abdominal pain	33 (9.8)	42 (12.2)	0.33	36 (10.7)	47 (13.7)	0.24
• Constipation	16 (4.7)	22 (6.4)	0.40	13 (3.8)	19 (5.5)	0.37
• Fatigue	19 (5.6)	23 (6.7)	0.63	19 (5.6)	28 (8.1)	0.23
• Paresthesia	14 (4.1)	22 (6.4)	0.23	17 (5.0)	22 (6.4)	0.51
• Peripheral sensory neuropathy	- (-)	- (-)	- (-)	21 (6.2)	13 (3.8)	0.16
• Urinary incontinence	8 (2.4)	19 (5.5)	**0.048**	16 (4.7)	38 (11.0)	**0.003**
• Urinary retention	2 (0.6)	38 (11.0)	**<0.0001**	2 (0.6)	34 (9.9)	**<0.0001**
• Dyspareunia	- (-)	- (-)	- (-)	21 (6.2)	19 (5.5)	0.75
• Pelvic pain	19 (5.6)	9 (2.6)	0.054	23 (6.8)	17 (4.9)	0.33
• Lymphedema	- (-)	- (-)	- (-)	35 (10.4)	36 (10.5)	1.00
• Hot flashes	- (-)	- (-)	- (-)	14 (4.1)	20 (5.8)	0.38

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Quality of Life and Sexual Health

Sexual-Vaginal Functioning (EORTC QLQ-CX24): Lower Score is Better			
	SH (Mean change score)	RH (Mean change score)	P-value
Month 3	4.41	16.03	p<0.0001
Month 6	0.93	11.85	p<0.0001
Month 12	0.94	9.16	p<0.0001
Sexual Pain (FSFI Pain Scale): Higher Score is Better			
	SH (Mean change score)	RH (Mean change score)	P-value
Month 3	0.03	-0.78	p=0.003
Month 6	0.10	-0.56	p=0.02
Month 12	0.35	-0.22	p=0.002

Significant differences between the two groups
All in favor of the simple hysterectomy group

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2023 ASCO® ANNUAL MEETING

Pembrolizumab + Chemotherapy versus Placebo + Chemotherapy for Persistent, Recurrent, or Metastatic Cervical Cancer: Final Overall Survival Results of KEYNOTE-826

Bradley J. Monk,[1] Nicoletta Colombo,[2,3] Krishnansu S. Tewari,[4] Coraline Dubot,[5] M. Valeria Caceres,[6] Kosei Hasegawa,[7] Ronnie Shapira-Frommer,[8] Pamela Salman,[9] Eduardo Yañez,[10] Mahmut Gümüş,[11] Mivael Olivera Hurtado de Mendoza,[12] Vanessa Samouëlian,[13] Vincent Castonguay,[14] Alexander Arkhipov,[15] Cumhur Tekin,[16] Kan Li,[16] Stephen M. Keefe,[16] Domenica Lorusso,[17] on behalf of the KEYNOTE-826 Investigators

[1]HonorHealth Research Institute, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA; [2]Gynecologic Oncology, European Institute of Oncology IRCCS and [3]Università degli Studi di Milano Bicocca, Milan, Italy; [4]Obstetrics & Gynecology, University of California, Irvine, Orange, CA, USA; [5]Oncologie Médicale, Institut Curie Saint Cloud, and GINECO, Paris, France; [6]Medical Oncology, Instituto de Oncologia Angel H. Roffo, Buenos Aires, Argentina; [7]Gynecologic Oncology, Saitama Medical University International Medical Center, Hidaka, Japan; [8]Ella Lemelbaum Institute for Immuno-Oncology, Sheba Medical Center, Ramat Gan, Israel; [9]Medical Oncology, Oncovida Cancer Center, Providencia, Santiago, Chile; [10]Medical Oncology, Universidad de la Frontera, Temuco, Chile; [11]Medical Oncology, Istanbul Medeniyet University Hospital, Istanbul, Turkey; [12]Medical Oncology, Instituto Nacional de Enfermedades Neoplásicas, Lima, Peru; [13]Gynecologic Oncology, Centre Hospitalier de l'Université de Montréal (CHUM), Centre de Recherche de l'Université de Montréal (CRCHUM), Université de Montréal, Montreal, QC, Canada; [14]Medical Oncology, Centre Hospitalier Universitaire de Québec, Université Laval, Quebec City, QC, Canada; [15]Oncology and Chemical Therapy, Medical Rehabilitation Center under the Ministry of Health of Russian Federation, Moscow, Russian Federation; [16]Oncology, Merck & Co., Inc., Rahway, NJ, USA; [17]Gynaecology Oncology Unit, Fondazione Policlinico Universitario A Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy

KEYNOTE-826: Randomized, Double-Blind, Phase 3 Study

308 pts

Key Eligibility Criteria

- Persistent, recurrent, or metastatic cervical cancer not amenable to curative treatment
- No prior systemic chemotherapy (prior radiotherapy and chemoradiotherapy permitted)
- ECOG PS 0 or 1

Stratification Factors

- Metastatic disease at diagnosis (yes vs no)
- PD-L1 CPS (<1 vs 1 to <10 vs ≥10)
- Planned bevacizumab use (yes vs no)

11% CPS < 1

R 1:1

Pembrolizumab 200 mg IV Q3W
for up to 35 cycles
+
Paclitaxel + Cisplatin or Carboplatin IV Q3W
for up to 6 cycles[a]
±
Bevacizumab 15 mg/kg IV Q3W

Placebo IV Q3W
for up to 35 cycles
+
Paclitaxel + Cisplatin or Carboplatin IV Q3W
for up to 6 cycles[a]
±
Bevacizumab 15 mg/kg IV Q3W

309 pts

End Points

- **Dual primary:** OS and PFS per RECIST v1.1 by investigator
- **Secondary:** ORR, DOR, 12-mo PFS, and safety

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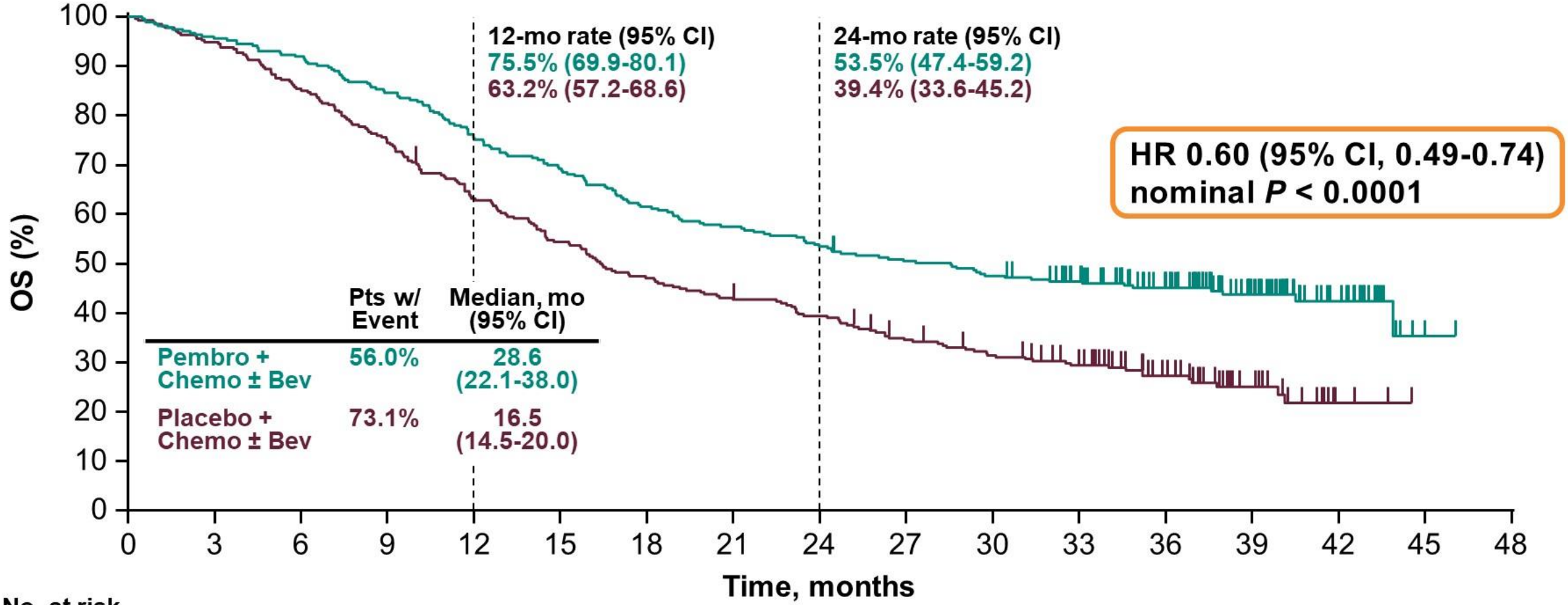
Protocol-Specified Final OS: PD-L1 CPS ≥1 Population



No. at risk

273	261	251	231	206	189	168	157	146	136	128	116	90	52	22	2	0
275	261	235	207	173	149	129	117	107	91	81	68	45	24	3	0	0

Data cutoff date: October 3, 2022.

Median (range) Follow-up[a]: 39.1 mo (32.1-46.5)

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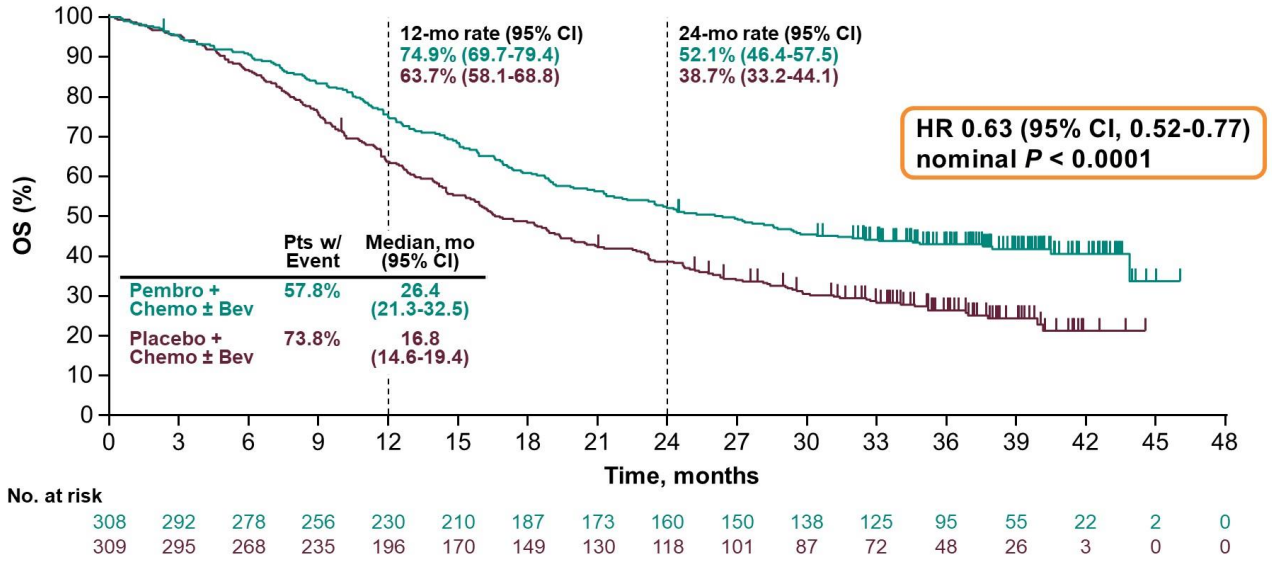
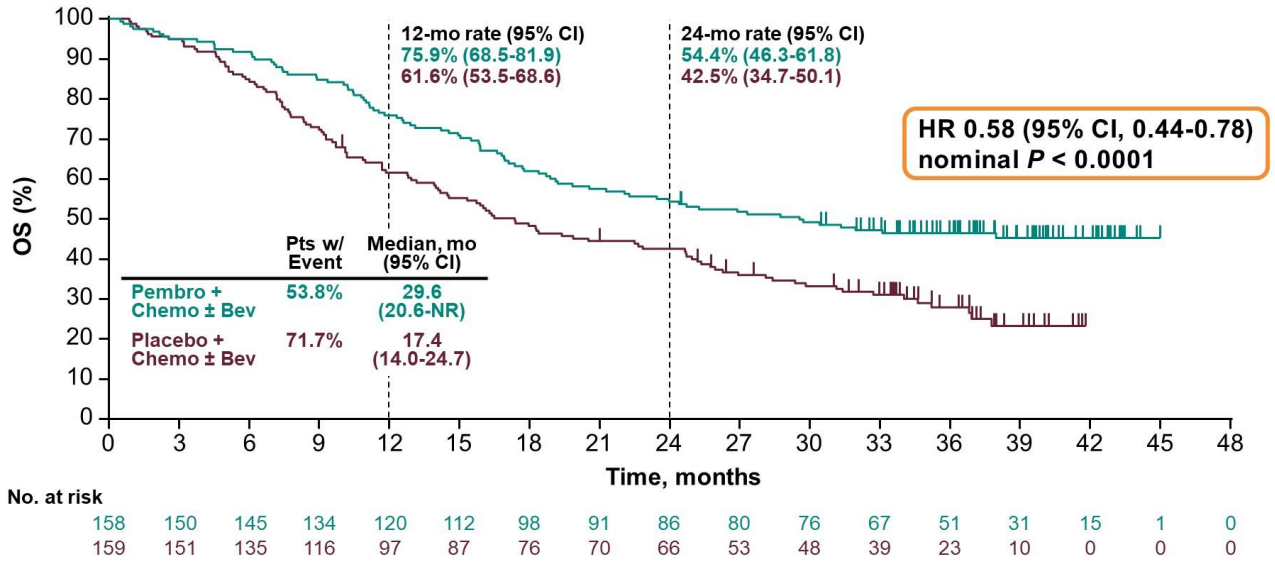
Protocol-Specified Final OS: All-Comer Population



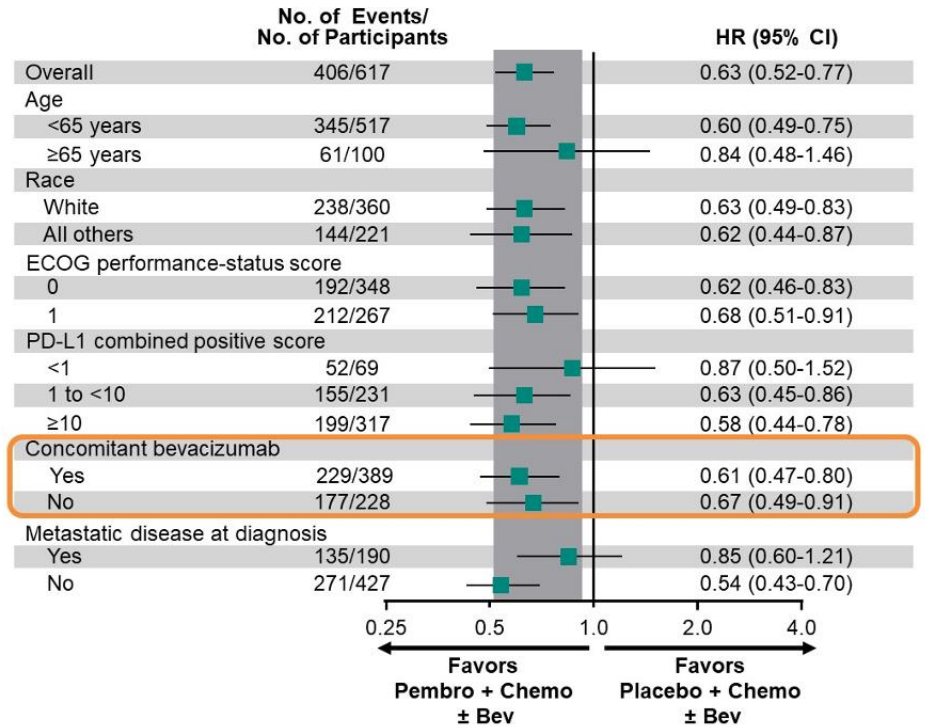
Data cutoff date: October 3, 2022.

Protocol-Specified Final OS: PD-L1 CPS ≥10 Population



Data cutoff date: October 3, 2022.

All-Comer Population



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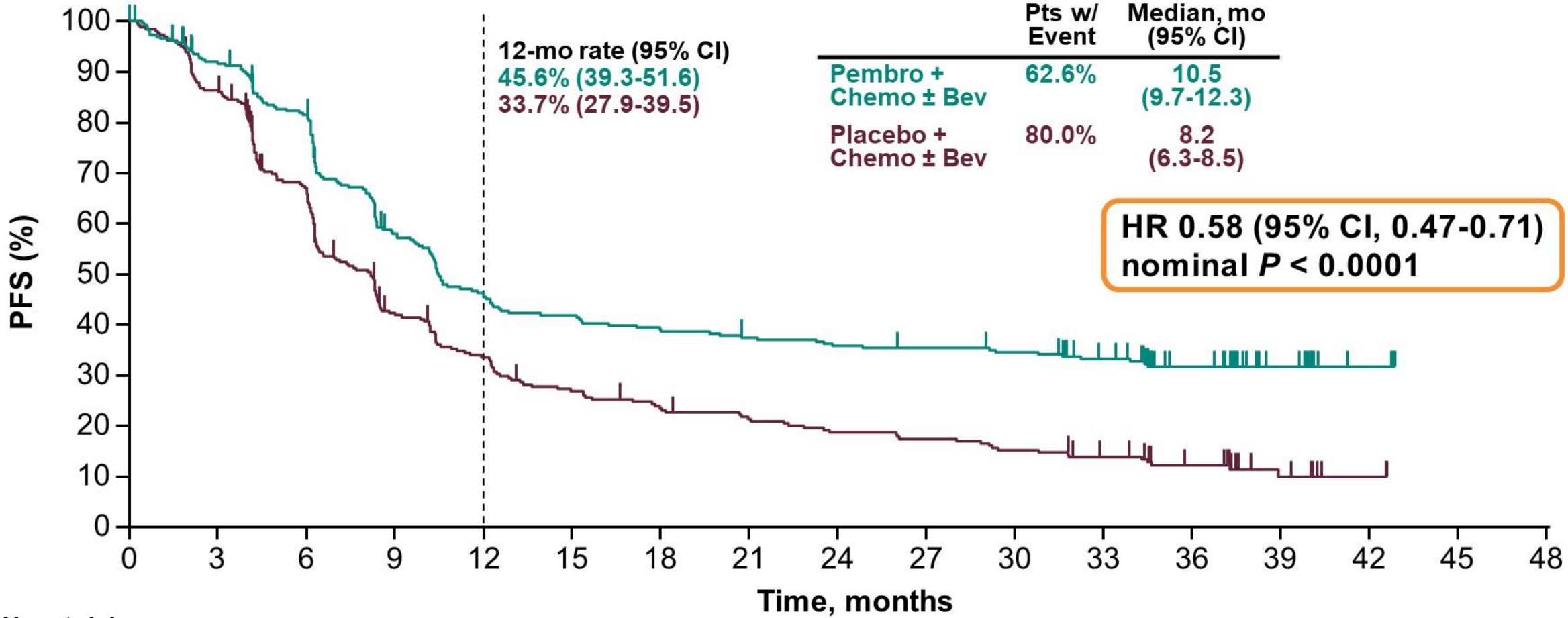
Protocol-Specified Final PFS: PD-L1 CPS ≥1 Population



No. at risk

273	238	208	144	113	104	97	92	88	86	83	70	46	25	6	0	0
275	229	170	103	81	64	55	49	43	40	35	28	18	7	2	0	0

Response assessed per RECIST v1.1 by investigator review. Data cutoff date: October 3, 2022.

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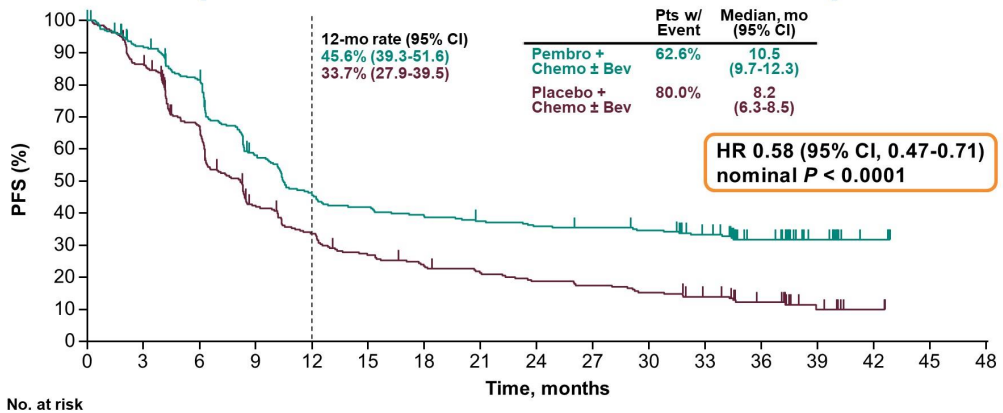
Protocol-Specified Final PFS: PD-L1 CPS ≥1 Population

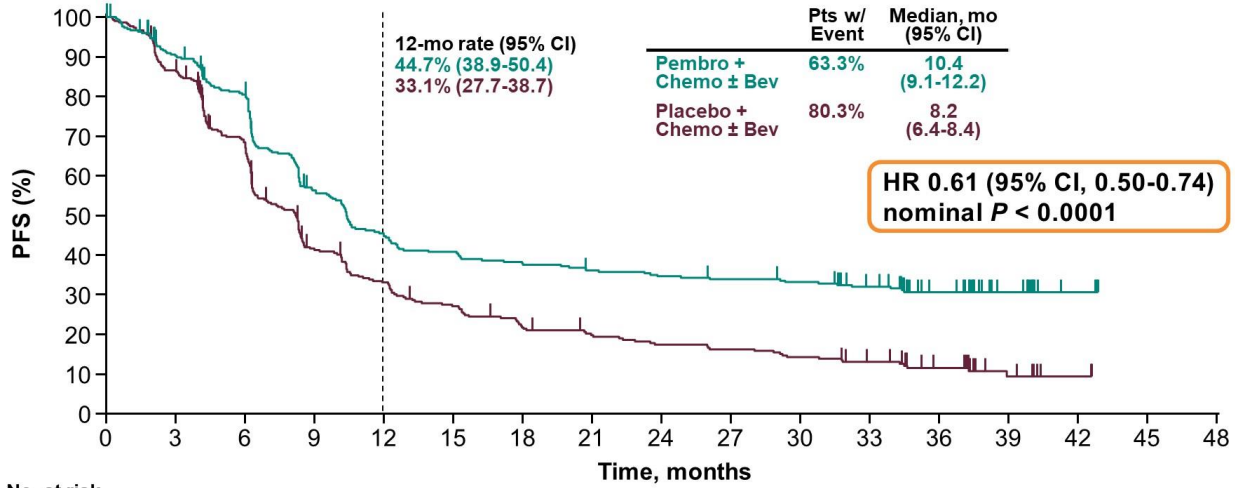


No. at risk

273	238	208	144	113	104	97	92	88	86	83	70	46	25	6	0	0
275	229	170	103	81	64	55	49	43	40	35	28	18	7	2	0	0

Response assessed per RECIST v1.1 by investigator review. Data cutoff date: October 3, 2022.

Protocol-Specified Final PFS: All-Comer Population

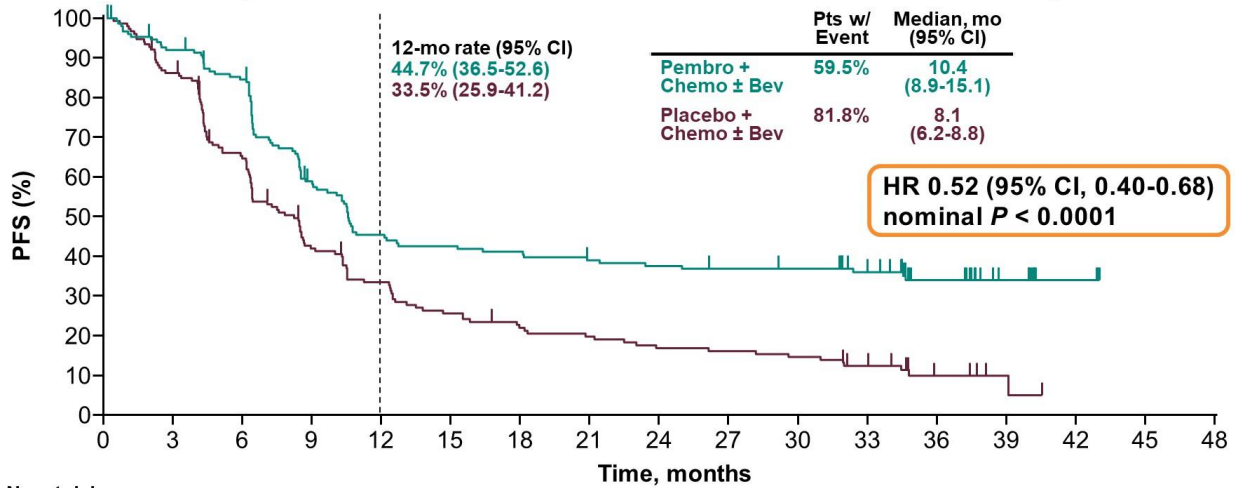


No. at risk

308	263	229	156	124	113	105	99	95	92	89	76	49	26	6	0	0
309	259	195	113	89	72	57	50	44	41	36	29	18	7	2	0	0

Response assessed per RECIST v1.1 by investigator review. Data cutoff date: October 3, 2022.

Protocol-Specified Final PFS: PD-L1 CPS ≥10 Population



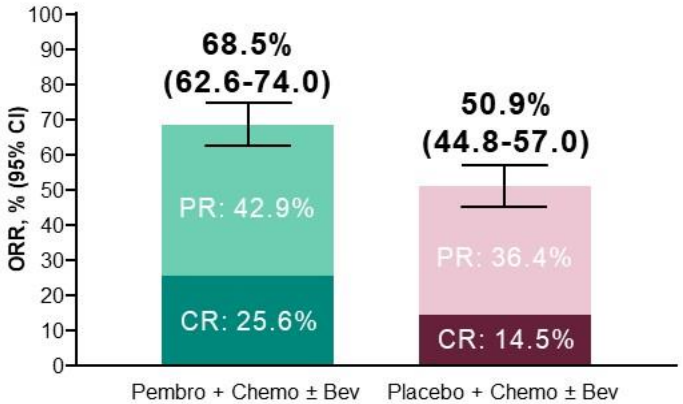
No. at risk

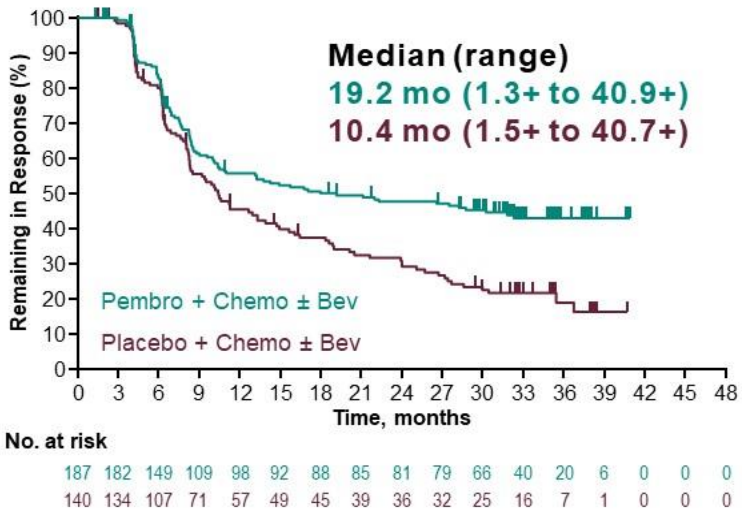
158	138	124	81	63	60	57	54	52	50	49	42	26	14	5	0	0
159	131	95	60	47	36	30	27	23	22	20	13	6	1	0	0	0

Response assessed per RECIST v1.1 by investigator review. Data cutoff date: October 3, 2022.

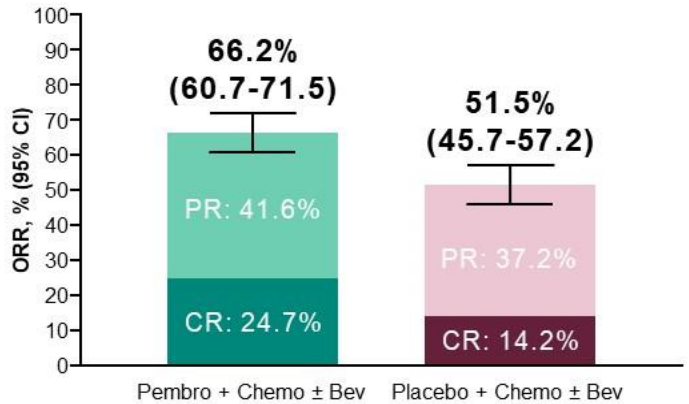
Protocol-Specified Final ORR and DOR: All Analysis Populations

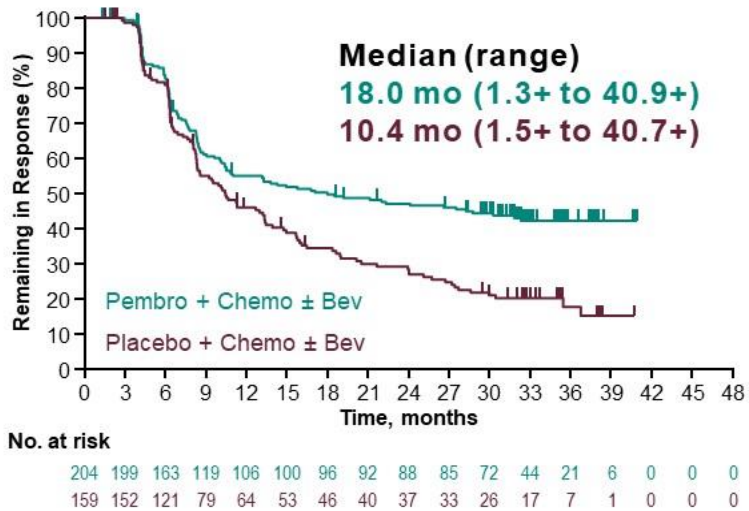
PD-L1 CPS ≥1



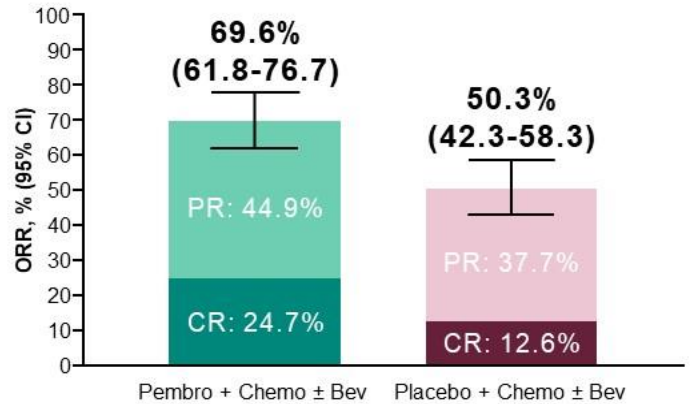


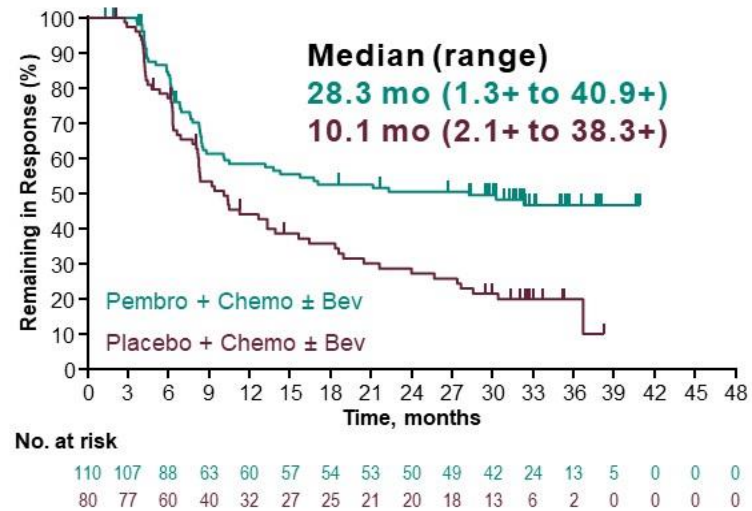
All-Comer





PD-L1 CPS ≥10





Response assessed per RECIST v1.1 by investigator review. Data cutoff date: October 3, 2022.

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Updated Adverse Events and Exposure

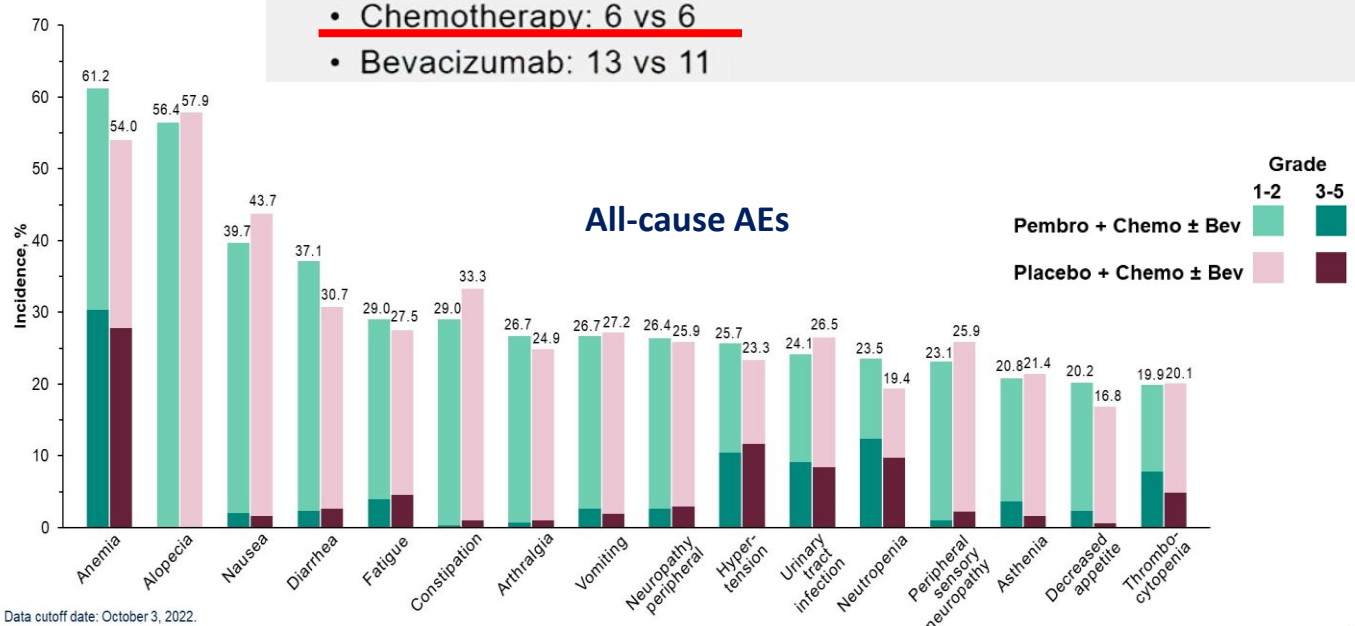
	All-Cause AEs		Treatment-Related AEs[a]		Immune-Mediated AEs[b]	
	Pembro Arm[c] (N = 307)	Placebo Arm[c] (N = 309)	Pembro Arm[c] (N = 307)	Placebo Arm[c] (N = 309)	Pembro Arm[c] (N = 307)	Placebo Arm[c] (N = 309)
Any grade	305 (99.3%)	307 (99.4%)	298 (97.1%)	300 (97.1%)	106 (34.5%)	51 (16.5%)
Grade ≥3	253 (82.4%)	233 (75.4%)	212 (69.1%)	201 (65.0%)	37 (12.1%)	9 (2.9%)
Serious	157 (51.1%)	132 (42.7%)	94 (30.6%)	73 (23.6%)	24 (7.8%)	7 (2.3%)
Led to death	16 (5.2%)	15 (4.9%)	2 (0.7%)[d]	4 (1.3%)[e]	2 (0.7%)[d]	0
Led to discontinuation						
Any treatment	125 (40.7%)	91 (29.4%)	102 (33.2%)	77 (24.9%)	20 (6.5%)	1 (0.3%)
All treatment	17 (5.5%)	15 (4.9%)	9 (2.9%)	6 (1.9%)	2 (0.7%)	0

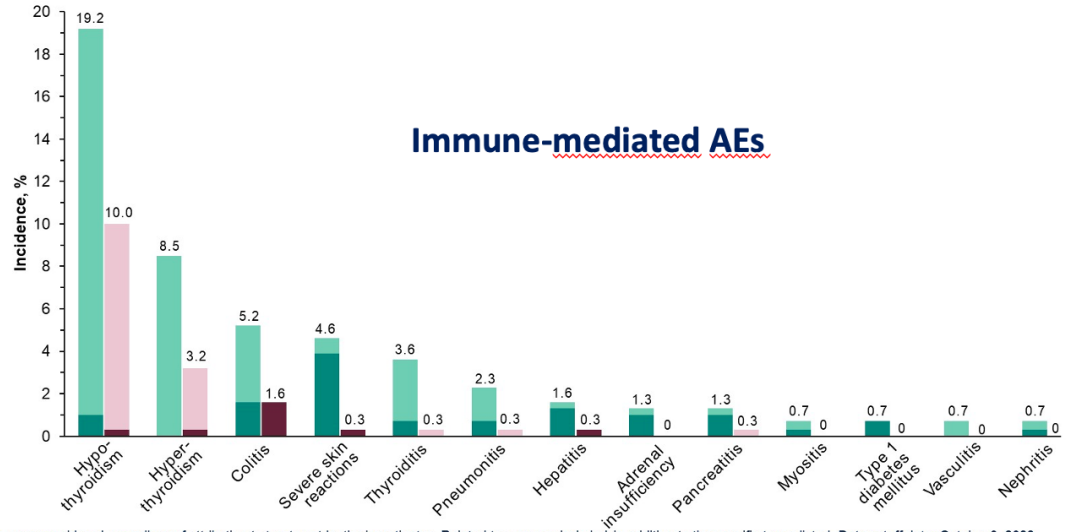
Median no. of cycles, pembro vs placebo arm

- Any treatment: 14 vs 11
- Pembrolizumab or placebo: 13 vs 11
- Chemotherapy: 6 vs 6
- Bevacizumab: 13 vs 11

Treatment duration, pembro vs placebo arm

- Median: 10.0 mo vs 7.7 mo
- Mean: 14.4 mo vs 10.8 mo





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GINECO

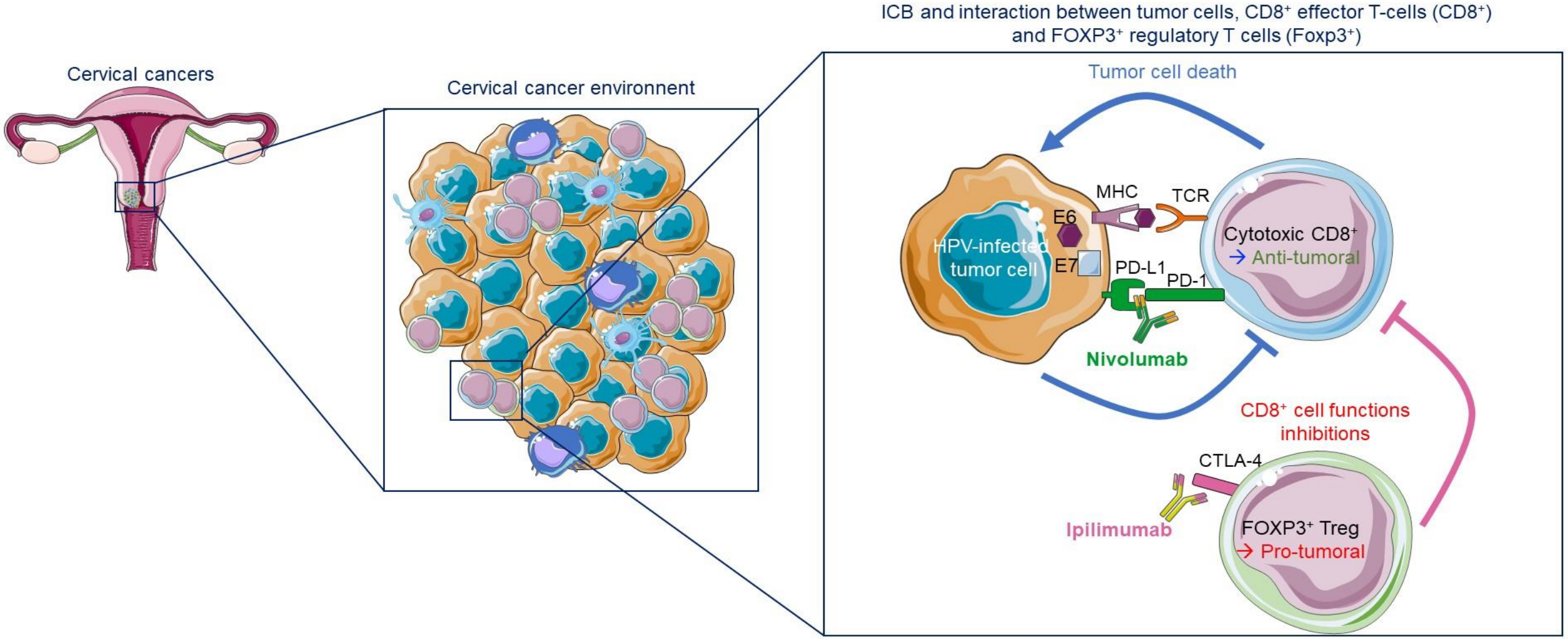
In situ immune impact of neo-adjuvant nivolumab + ipilimumab combination (ICB) before standard chemoradiation therapy for FIGO IB3-IVA cervical squamous carcinoma patients.

COLIBRI trial, a GINECO study.

Isabelle RAY-COQUARD, Marie-Christine Kaminsky-Forrett, Ryotaro Ohkuma, Aymeric De Montfort, Florence Joly, Isabelle Treilleux, Sarah Ghamry-Barrin, Diana Bello-Roufai, Pierre Saintigny, Antoine Angelergues, Lucas Michon, Anne-Claire Hardy-Bessard, Alexandra Lainé, Aude-Marie Savoye, Justine Berthet, Christophe Caux, Fabrice Lecuru, Bertrand Dubois, Sarah Lagarde Bétrian.

Rationale

- A high tumor CD8+/FOXP3+ cell ratio is associated with better clinical outcome after neoadjuvant chemotherapy in cervical cancer patients[2]



1. How does neo adjuvant double PD-1/CTLA4 blockade impacts the immune response in cervical cancer ?
2. Is sequencing ICB before and after RTCT impacting on immune response and efficacy ?

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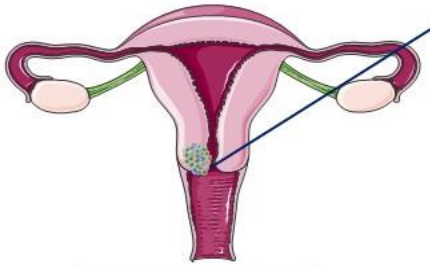
COLIBRI inclusion criteria & Study design



Cervical cancer
- Women aged ≥18 years
- Histologically confirmed cervical (adeno)squamous carcinoma
- LACC (FIGO 2018) stage IB3-IVA
- ECOG performance status of 0 or 1
- Single arm pilot study

MRI/PET — MRI/PET — MRI/PET — Surgery of residual disease (optional) — MRI/PET

Screening <28d | **Neo-adjuvant phase** | **RTCT*** 5-8 weeks | *Delay of 4-6 weeks* | **Maintenance with nivolumab (6 months)** | **EOT** | **Follow-up**

D1C1 — D15C1 — D-1 of RTCT — 4 weeks post RTCT — D1C4

*1 — *2

Nivolumab 3mg/kg
Ipilimumab 1mg/kg

Nivolumab 480mg, q4w

- *Painful process, biopsy refused by 13 (32%) of the patients*
- ***26 (96%) without tumor cells***
- *Microenvironment analysis was not done so far*

Tumor biopsy
Blood sample

*1 optional *cervical tumor sample during the surgery*
*2 *mandatory blood sample and optional biopsy at progression*

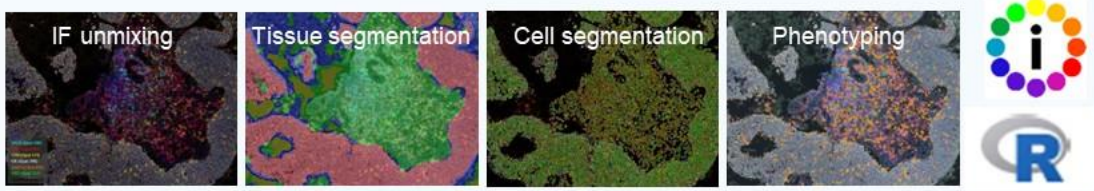
Methods – multi-IF and HTG

7-colors multiplex immunofluorescence tissue imaging (multi-IF)[1,2]:

CD3-CD8-CD20-Foxp3-Ki67-CK-DAPI

↓

Digital image analysis by machine learning



↓

Densities (cells/mm²)
- Total and proliferating (Ki67⁺) CD8⁺ (CD3⁺CD8⁺Foxp3⁻)
- Total Foxp3⁺ (CD3⁺Foxp3⁺)

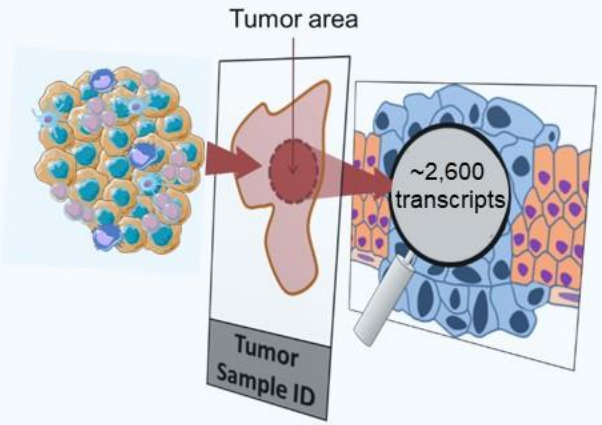
Ratio
- Total CD8⁺ / Total Foxp3⁺
- Proliferating CD8⁺ / Proliferating Total Foxp3⁺

[1]Small M, et al. *Acta Neuropath*. 2018;135:569-579
[2]Plaschka M, et al. *J Immunother Cancer*. 2022

Transcriptomic analysis

High-Throughput Genomic sequences (HTG):

Evaluation of the 'HOT' score as biomarker for immunologically active tumors which may benefit from immunotherapies[3]



HOT signature gene list: CCL19, CCR2, CCR4, CCR5, CD27, CD40LG, CD8A, CXCL10, CXCL11, CXCL13, CXCL9, CXCR3, CXCR6, FASLG, FGL2, GZMA, GZMH, IDO1, IFNG, IRF8, LAG3, LYZ, MS4A1, PDCD1, TBX21, TLR7, TLR8

[3]Foy JP, et al. *Eur J Can*. 2022;174:287-298.

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Objectives of the COLIBRI trial

- **Primary objective:**
  To measure the CD8⁺/FOXP3⁺ lymphocyte ratio in pre- versus post-ICB therapy biopsies in patients treated with neo-adjuvant combination of nivolumab + ipilimumab, before starting standard RTCT.

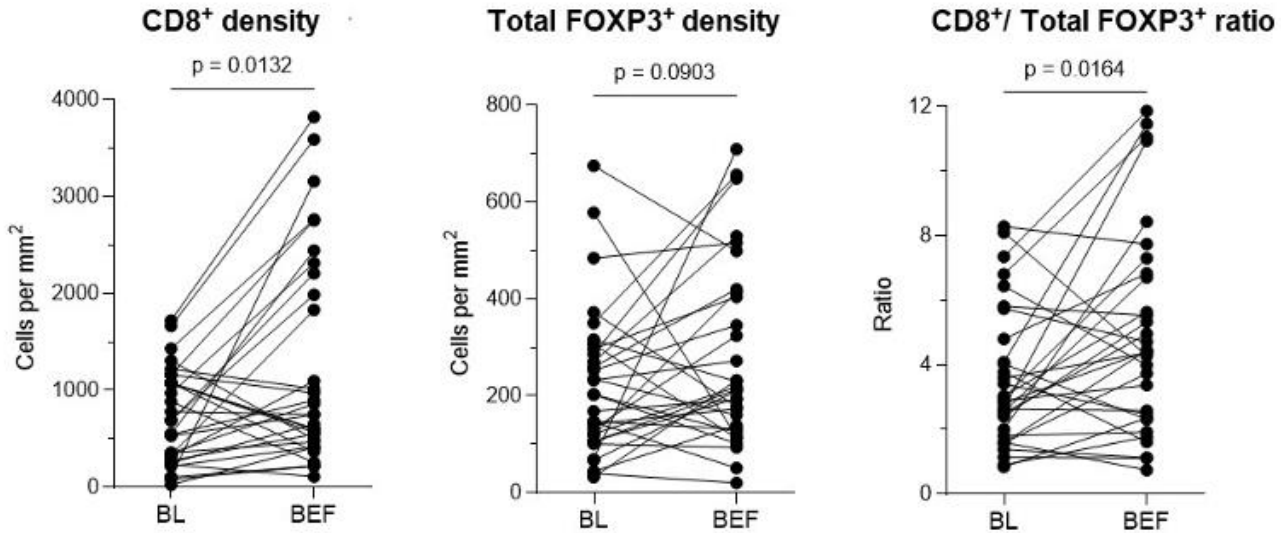
  → ***Primary endpoint:*** *CD8⁺/FOXP3⁺Treg cell relative change between pre- and post-ICB biopsies by multiplex-immunofluorescence (multi-IF) tissue imaging*

- **Secondary objectives:**
  - Evolution of the immune microenvironment (CD8⁺, FOXP3⁺Treg, DCs, MPs,…) before & after RTCT, and at progression → multi-IF and HTG
  - Objective Response Rate (ORR) by RECIST 1.1 criteria before & after RTCT, and at EOT for local tumor and global response
  - Correlation between clinical activity assessment and biological changes of the immune microenvironment
  - Safety
  - *Progression Free Survival and Overall Survival at 3 years*
  - *Other exploratory translational research on immune microenvironment and HPV molecular signatures*

Clinical endpoints(OS, PFS) expected in 2025

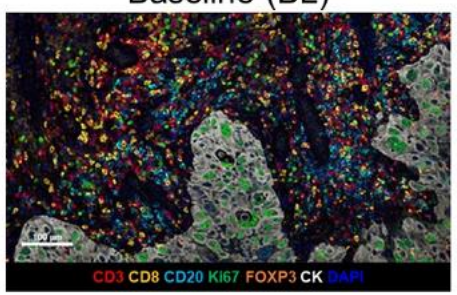
Results – relative changes before/after ICB by multi-IF

Neo-adjuvant double ICB significantly increases tumor-associated CD8⁺T cells and CD8⁺/FOXP3⁺ ratio



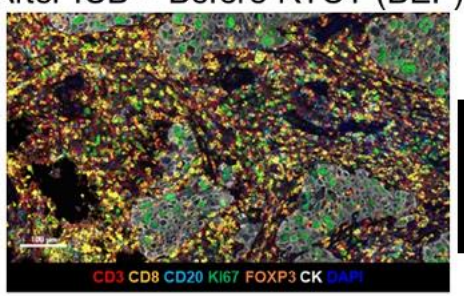
009-04

Baseline (BL)



Ipi + Nivo

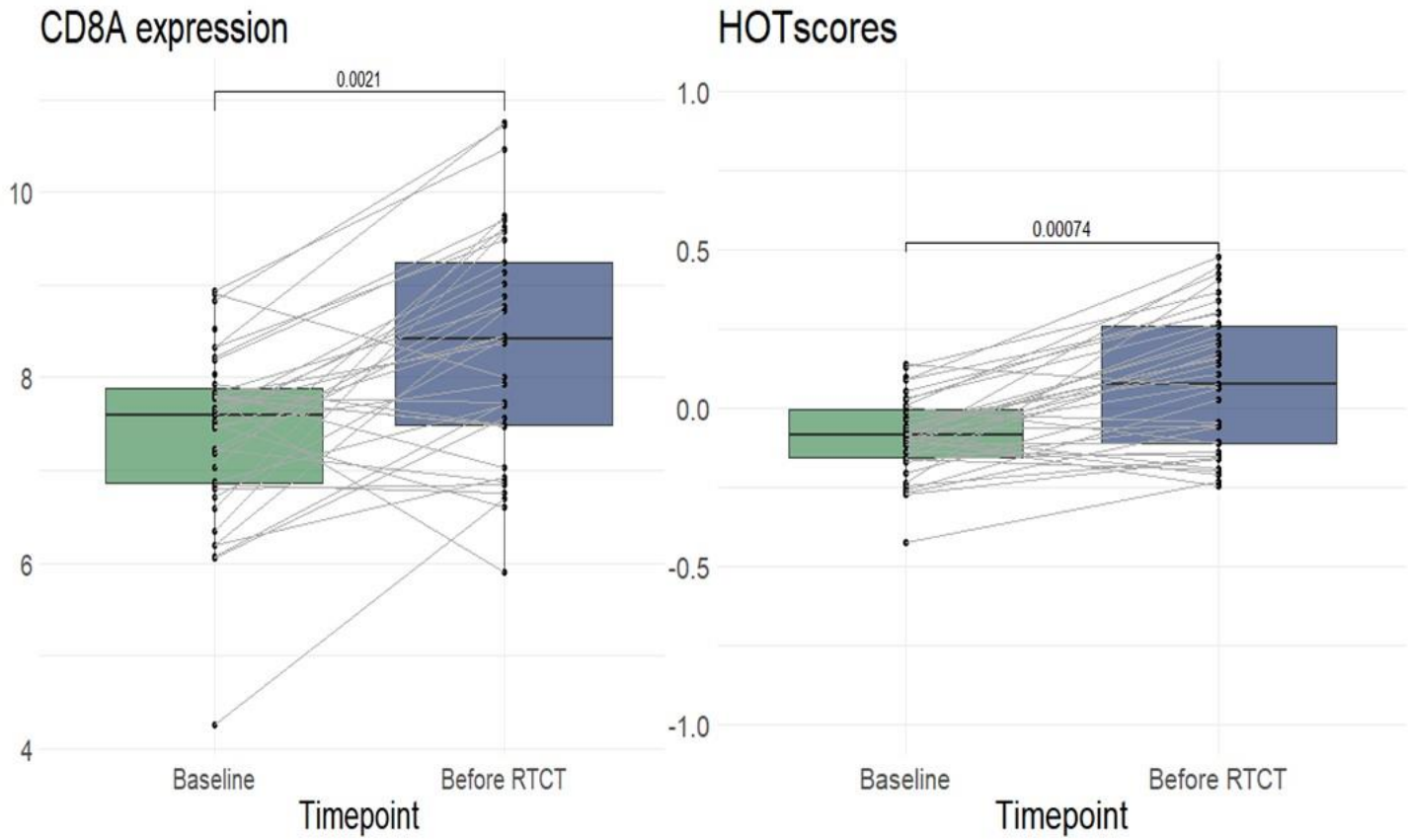
After ICB = Before RTCT (BEF)



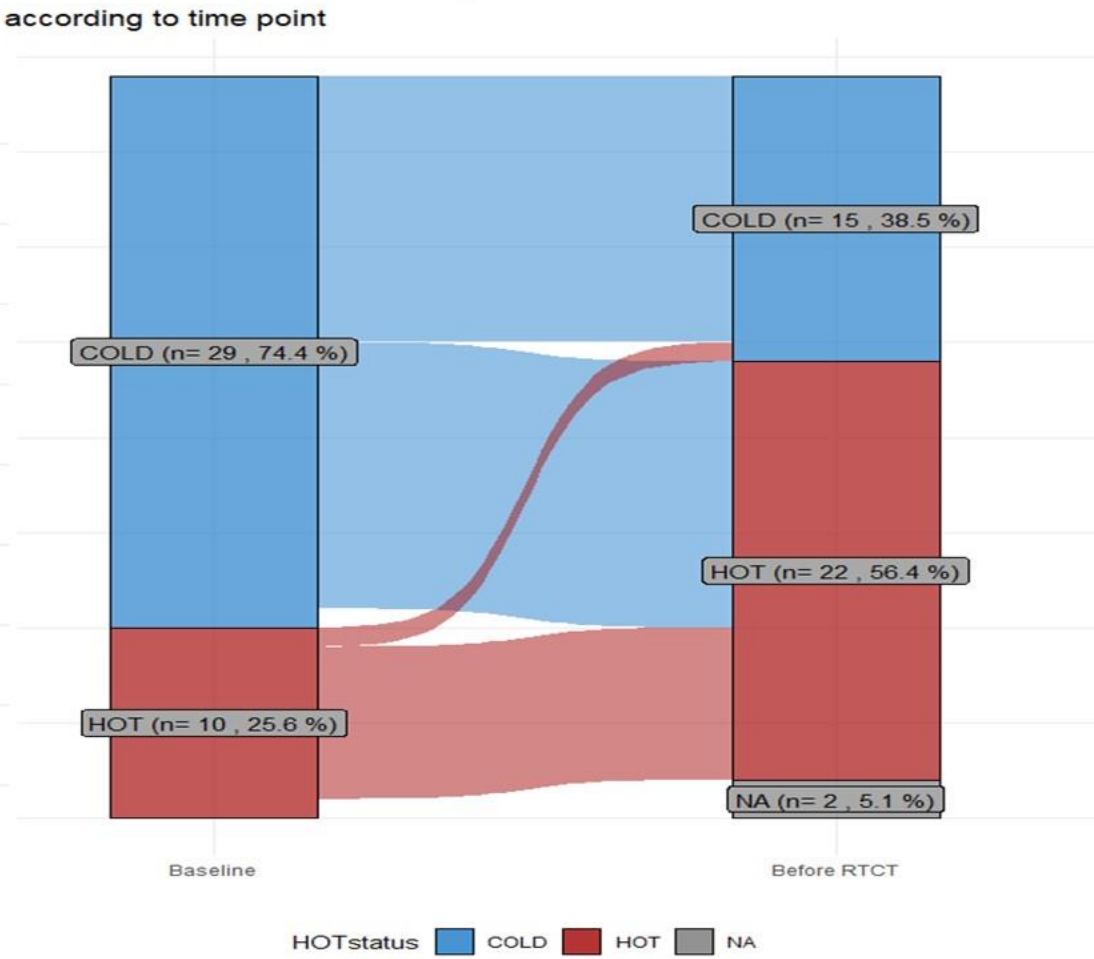
Increased immune cell density (>>CD8+)

Results – HTG

Significant increase of the *CD8A* gene expression and the 'HOT' score after ICB was observed



Evolution of the 'HOT' score after neo-adjuvant ICB



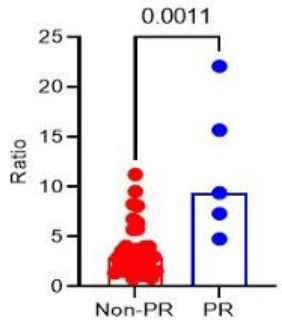
Results – correlation with response rate

Elevated CD8⁺/FOXP3⁺ ratio at baseline correlate with partial response before RTCT

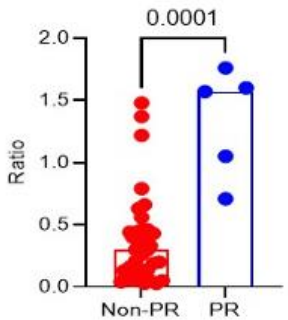
Baseline

Response before RCT

CD8⁺/ Total FOXP3⁺ ratio



Ki67⁺ CD8⁺/ Total FOXP3⁺ ratio

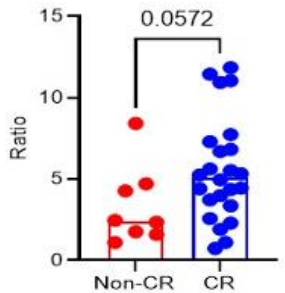


Elevated proliferative CD8⁺/FOXP3⁺ ratio correlate with CR at the end of maintenance therapy

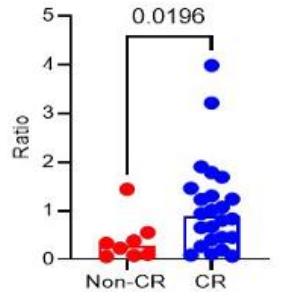
Before RTCT

Response at EOT

CD8⁺/ Total FOXP3⁺ ratio

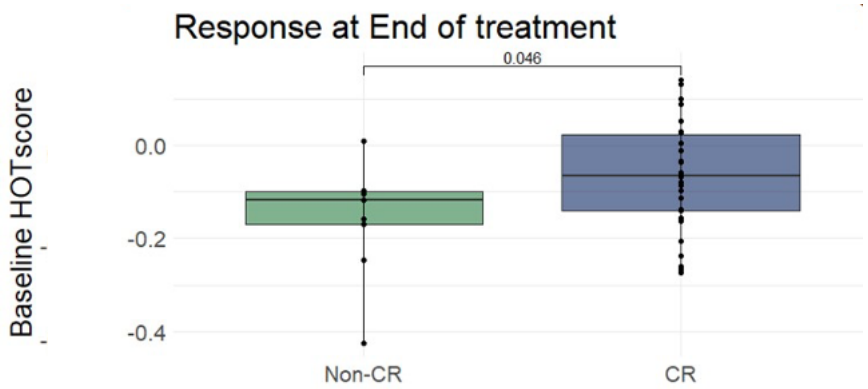


Ki67⁺ CD8⁺/ Total FOXP3⁺ ratio



The 'HOT' score at baseline correlates with complete response at the end of maintenance therapy

Baseline



Results – efficacy by response rate after neo-adjuvant ICB, post RTCT and end of maintenance

RESPONSE	RR	Before RTCT N (%)		Post RTCT N(%)		End of maintenance	
Local control	CR	-		27	(68)	34	(85)
	PR	**6**	**(15)**	12	(30)	3	(8)
	SD	32	(80)	1	(2)	1	(2)
	PD	**2**	**(5)**	-		2	(5)
Global response	CR	-		26	(65)	31	(78)
	PR	5	(13)	13	(33)	5	(12)
	SD	33	(82)	1	(2)	-	
	PD	2	(5)	-		**4**	**(10)**

3 pts with FIGO IIIC
4 pts have no change before/after ICB for:
- CD8+ infiltrate
- CD8+/Foxp3 ratio
- Cold 'HOT' score

RESPONSE	FIGO STAGE	COMPLETE RESPONSE RATE
Global response	FIGO I/II	81%
	FIGO III/IV	74%

2023 ASCO ANNUAL MEETING

NRG ONCOLOGY

Advancing Research. Improving Lives.™

Incorporation of triapine (T) with cisplatin chemoradiation (CRT) for locally advanced cervical and vaginal cancer: Results from NRG-GY006, a phase III randomized trial

Charles A. Leath, III, Wei Deng, Loren K. Mell, Debra L. Richardson, Joan L. Walker, Laura L. Holman, Jayanthia S. Lea, Sudha R. Amarnath, Luis J. Santos-Reyes, Rebecca C. Arend, Jyoti Mayadev, Naresh Jegadessh, Paul DiSilvestro, Hye Sook Chon, Sharad A. Ghamande, Allison M. Quick, Junzo P. Chino, Helen Mackay, Carol Aghajanian, Bradley J. Monk on behalf of NRG Oncology

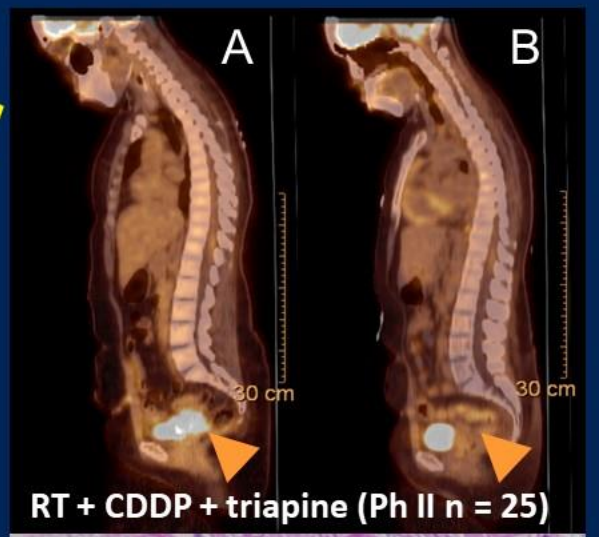
PRESENTED BY: Charles A. Leath, III, MD, MSPH, Director Division of Gynecologic Oncology

Triapine (3-AP) in cervical cancer

- Enzyme catalyzing deoxyribonucleotides from ribonucleotides
- RNR over activity may be important in cervical cancer
- Triapine (3-AP) – RNR inhibitor evaluated in patients with cervical cancer
- 500-1000X more potent inhibitor of ribonucleotide reductase than hydroxyurea

Phase 1 trial (N=10 Cx Ca + 1 Ut Sarcoma patients)[1]
- LACC – Stage IB2–IVB
- MTD 25mg/m^2 IV 3x per week
- 100% CCR, median DFS 18 months (6-32 mo)

Phase 2 trial (N=22 Cx Ca + 3 Vaginal Ca)[2]
- LACC – Stage IB2–IVB, Vaginal – Stage II–IV
- 96% Clinical response (95% CI 80-99%)
- 23/24 patients with PET based metabolic response



96% metabolic CR response

[1]Kunos CA et al. *Clin Cancer Res* 2010
[2]Kunos CA et al. *Gynecol Oncol* 2013

NRG GY-006 Study Schema

Patients with cervical or vaginal cancer suitable for chemoradiation with curative intent:

- **Cervical - FIGO 2009 Stage IB2 (>4cm*), II, IIIB, IVA**
- **Vaginal Stage II-IVA**
- **ECOG 0-2**
- **Squamous cell ca adenocarcinoma or adenosquamous ca**
- **No + para-aortic nodes on pre-treatment PET/CT**

R

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Concurrent Chemoradiation (CRT)

- **Radiation – 45Gy/25 fractions**
- **Weekly Cisplatin 40mg/m² x5***
- **Max dose 70mg**
- **Days 2,9,16,23,30 *(Additional dose on day 36 permissible)**
- **Brachytherapy**

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Concurrent Chemoradiation (CRT) + Triapine 3x weekly

- **TRIAPINE 25 mg/m² Max Dose 50mg**
- **Days 1,3,5,8,10,12,15,17,19,22,24, 26,29,31,33 (15 infusions)**
- **Weekly Cisplatin 40mg/m²**
- **Maximum dose 70mg**

Primary Endpoint

Overall Survival

Secondary Endpoints

Progression-free survival

Tertiary Endpoints

Adverse Events

KBP

PET/CT CMR at 3 months

Stratification Factors

- Type of brachytherapy – LDR vs. HDR
- Radiation modality – IG-IMRT (Yes vs/ No)
- FIGO 2009 stage: Stage II</= versus ≧ Stage III

* Original > 5cm

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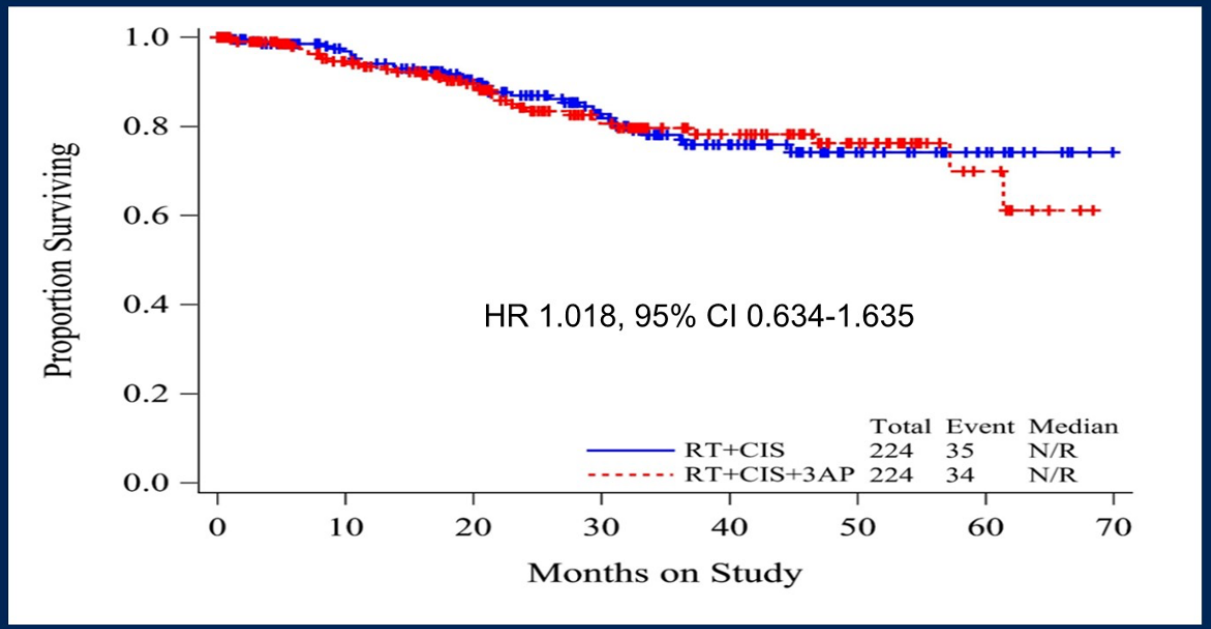
450 randomised (2016 – 2022)

Median follow-up 28 months

Overall Survival



No differences in Grade 3-5 toxicities: CRT =52% and CRT +T= 49%

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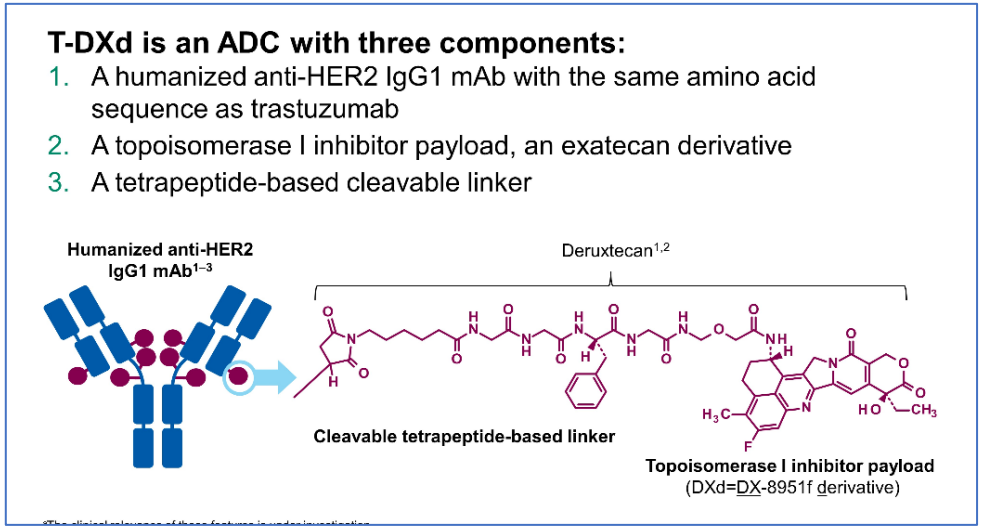
Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: DESTINY-PanTumor02 interim results

Funda Meric-Bernstam

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

June 5, 2023

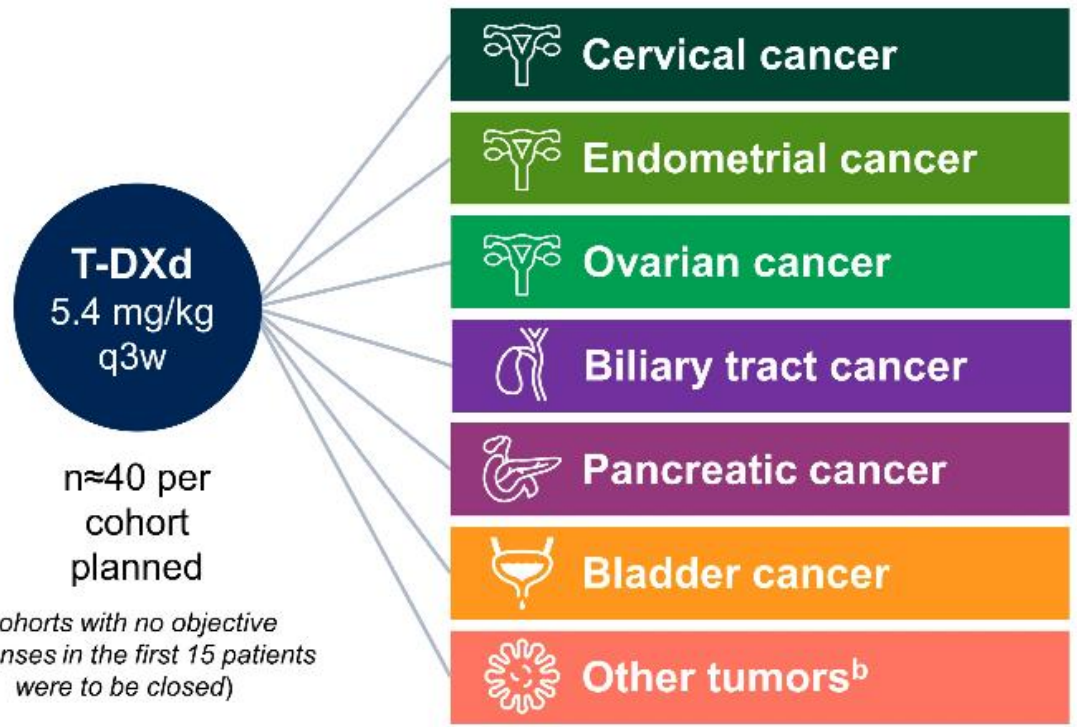
Additional authors: Vicky Makker, Ana Oaknin, Do-Youn Oh, Susana Banerjee, Antonio González-Martín, Kyung Hae Jung, Iwona Ługowska, Luis Manso, Aránzazu Manzano, Bohuslav Melichar, Salvatore Siena, Daniil Stroyakovskiy, Chiedozie Anoka, Yan Ma, Soham Puvvada, Jung-Yun Lee



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

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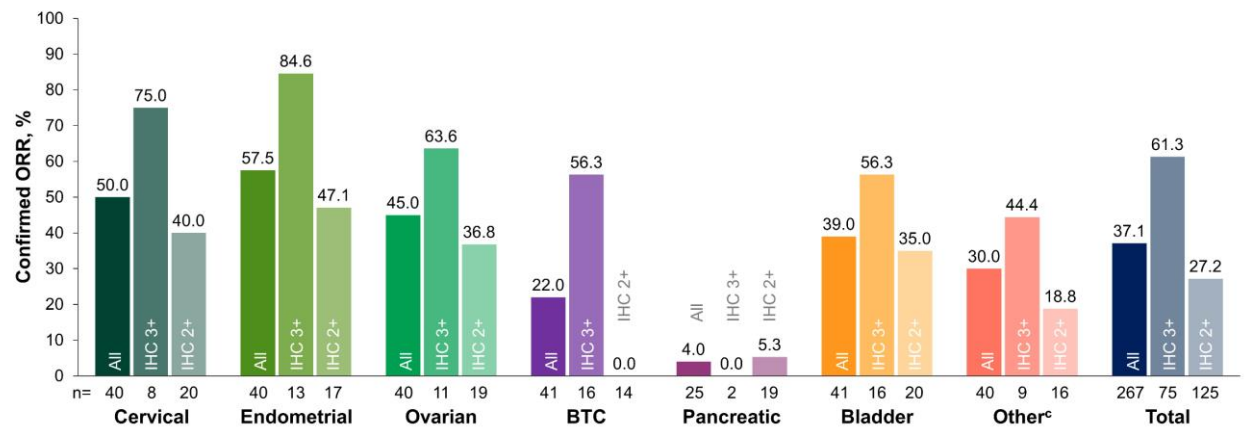
Efficacy endpoints: ORR, DCR and DOR

		Cervical (n=40)	Endometrial (n=40)	Ovarian (n=40)	BTC (n=41)	Pancreatic (n=25)	Bladder (n=41)	Other (n=40)	All patients (N=267)
Investigator assessment									
ORR, n (%)		**20 (50.0)**	**23 (57.5)**	**18 (45.0)**	**9 (22.0)**	**1 (4.0)**	**16 (39.0)**	**12 (30.0)**	**99 (37.1)**
Best overall response, n (%)	Complete response	2 (5.0)	7 (17.5)	4 (10.0)	1 (2.4)	0	1 (2.4)	0	15 (5.6)
	Partial response	18 (45.0)	16 (40.0)	14 (35.0)	8 (19.5)	1 (4.0)	15 (36.6)	12 (30.0)	84 (31.5)
	Stable disease	12 (30.0)	13 (32.5)	14 (35.0)	25 (61.0)	17 (68.0)	18 (43.9)	24 (60.0)	123 (46.1)
	PD	7 (17.5)	4 (10.0)	7 (17.5)	7 (17.1)	7 (28.0)	7 (17.1)	3 (7.5)	42 (15.7)
	Not evaluable	1 (2.5)	0	1 (2.5)	0	0	0	1 (2.5)	3 (1.1)
DCR[a] at 12 weeks, n (%)		27 (67.5)	32 (80.0)	28 (70.0)	27 (65.9)	9 (36.0)	29 (70.7)	30 (75.0)	182 (68.2)
Median DOR, months (95% CI)		9.8 (4.2–NE)	NR (9.9–NE)	11.3 (4.1–NE)	8.6 (2.1–NE)	NR	8.7 (4.3–11.8)	NR (4.1–NE)	11.8 (9.8–NE)
Independent central review: ORR, n (%)		16 (40.0)	21 (52.5)	17 (42.5)	11 (26.8)	3 (12.0)	17 (41.5)	13 (32.5)	98 (36.7)

Objective Response Rate by HER2 status



	All patients (N=99)	IHC 3+ (n=46)	IHC 2+ (n=34)
Median DOR, months (95% CI)	11.8 (9.8–NE)	22.1 (9.3–NE)	9.8 (4.2–12.6)

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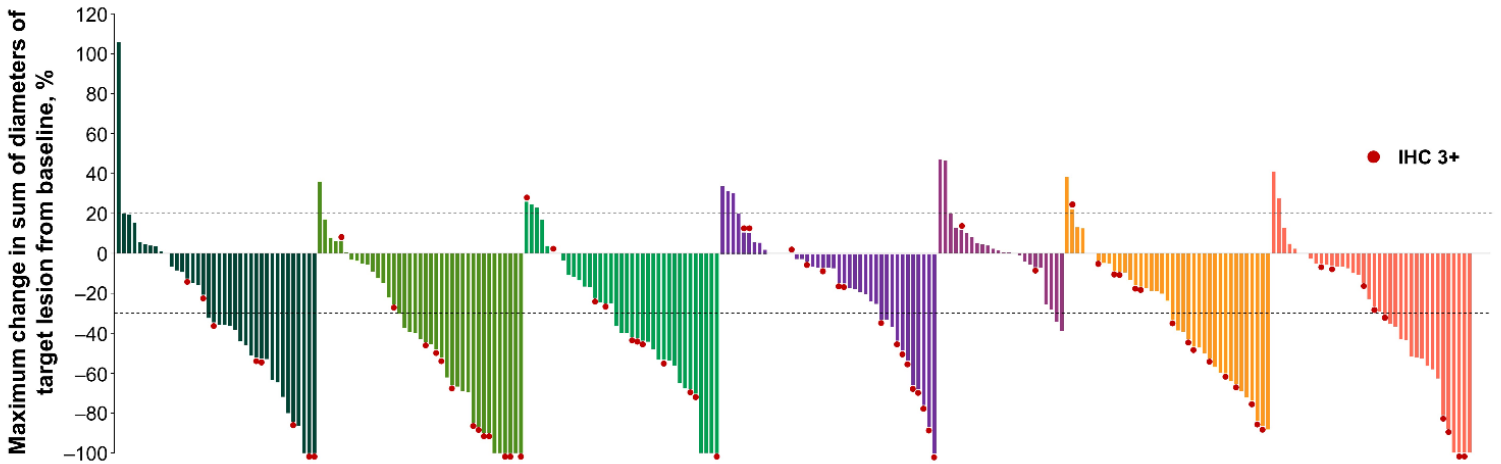
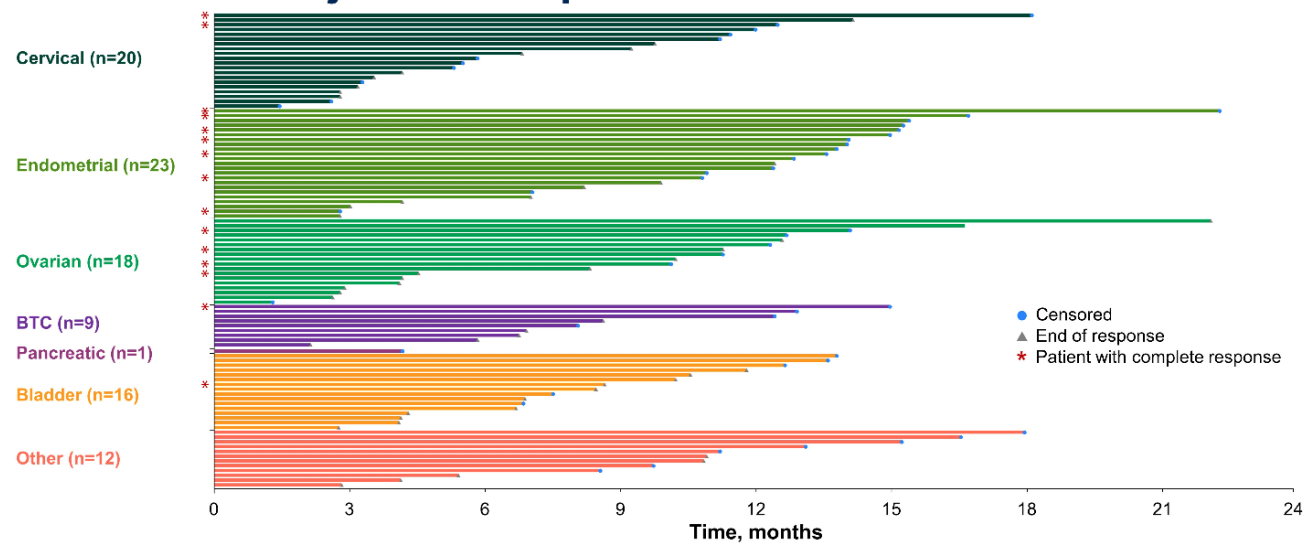
Best Percentage Change in Target Lesion From Baseline



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

Duration of Objective Response



Kaplan-Meier estimate of response at 12 months (%)	Cervical	Endometrial	Ovarian	BTC	Pancreatic	Bladder	Other	All
	47.6	72.3	45.8	41.7	0	23.2	53.6	49.6

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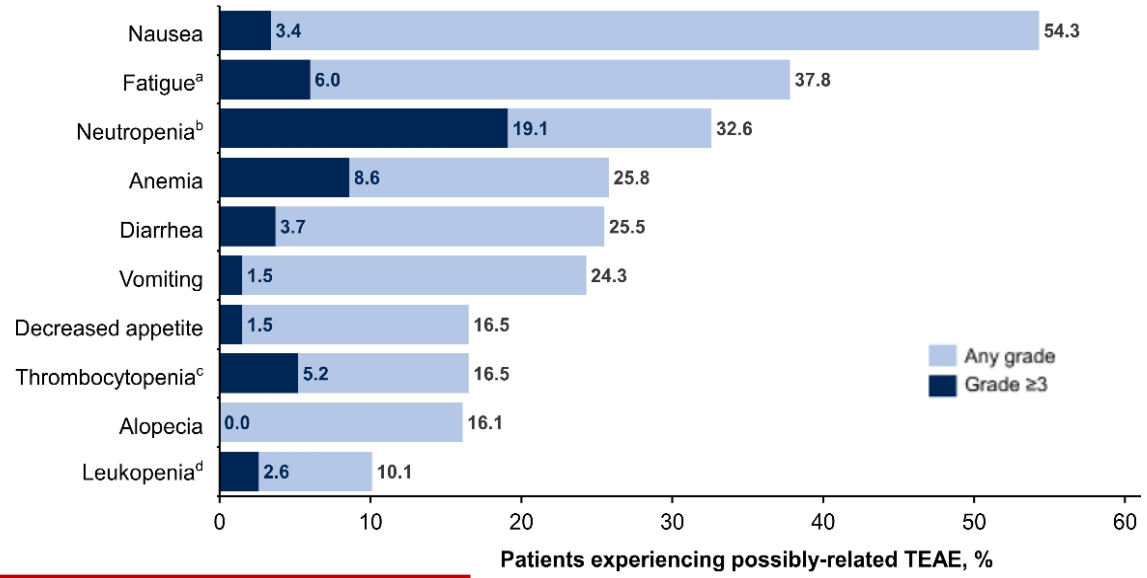
Overall Safety Summary

n (%)	All patients (N=267)
Any drug-related TEAEs	225 (84.3)
Drug-related TEAEs Grade ≥3	103 (38.6)
Serious drug-related TEAEs	32 (12.0)
Drug-related TEAEs associated with dose discontinuations	22 (8.2)
Drug-related TEAEs associated with dose interruptions	49 (18.4)
Drug-related TEAEs associated with dose reductions	50 (18.7)
Drug-related TEAEs associated with deaths	2 (0.7)[a]

Drug-Related TEAEs in ≥10% of Patients



Adverse Events of Special Interest

ILD/pneumonitis adjudicated as T-DXd–related

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
All patients (N=267)	6 (2.2)	12 (4.5)	1 (0.4)	0	1 (0.4)	20 (7.5)

Left ventricular dysfunction[a]

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
Ejection fraction decreased						
All patients (N=267)	1 (0.4)	4 (1.5)	1 (0.4)	0	0	7 (2.6)[b]
Cardiac failure						
All patients (N=267)	0	0	1 (0.4)	0	0	1 (0.4)

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Grazie MaNGO Mario Negri Gynecologic Oncology !!!