2023 Updates in Gynecologic Oncology: Research into Practice

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Agenda

Approach to Advanced, Recurrent, or Metastatic Endometrial Cancer

-Incorporation of immune checkpoint inhibitors

Treatment for newly diagnosed ovarian cancer

-New data related to HIPEC

Surgery for early cervical cancer

-Is less non-inferior

Recurrent ovarian cancer

-Something new beyond chemotherapy

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2023 ASCO ANNUAL MEETING

Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer: Outcomes by Blinded Independent Central Review of the RUBY trial (ENGOT-EN6-NSGO/GOG3031/RUBY)

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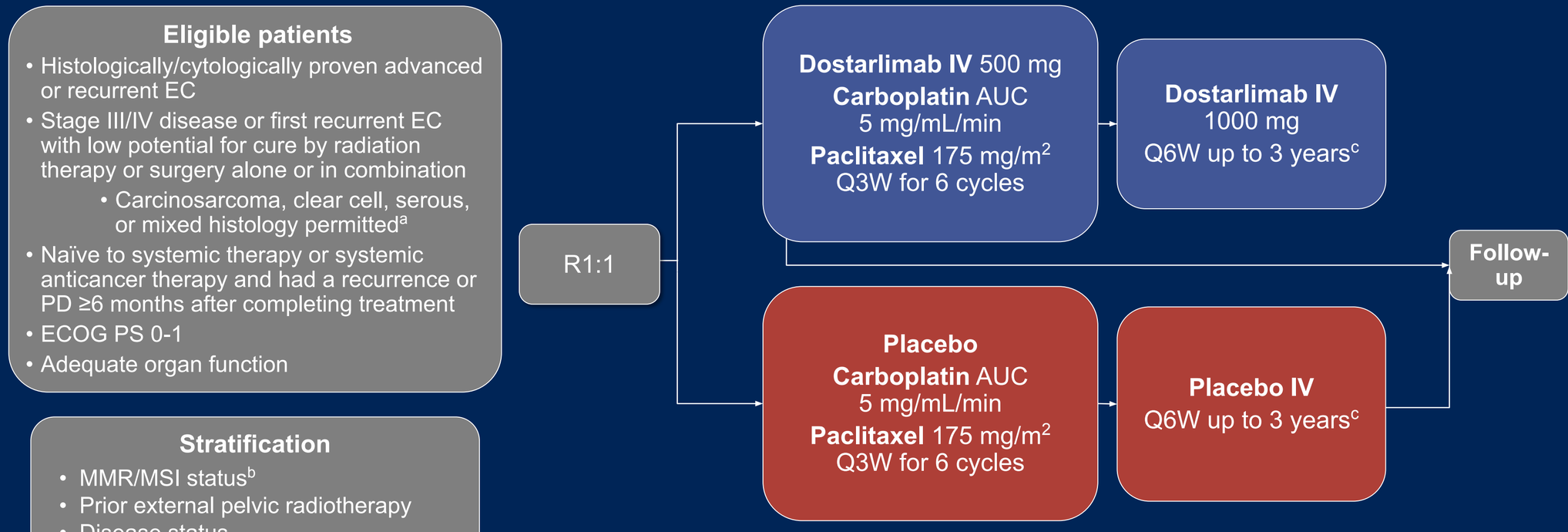
*Current affiliation. Affiliation at time of study Arizona Center for Cancer Care, Creighton University School of Medicine Phoenix, AZ, USA

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



Primary endpoint

- PFS by INV per RECIST v1.1
- OS

Secondary endpoints

- PFS by BICR per RECIST v1.1
- PFS2
- ORR
- DOR
- DCR
- HRQOL/PRO
- Safety

On-study imaging assessments are to be performed Q6W (±7 days) from the randomization date until Week 25 (Cycle 8), followed by Q9W (±7 days) until Week 52. Subsequent tumor imaging is to be performed every 12 weeks (±7 days) until radiographic PD is documented by Investigator assessment per RECIST v1.1 followed by one additional imaging 4-6 weeks later, or subsequent anticancer therapy is started, whichever occurs first. Thereafter, scans may be performed per standard of care.
[a]Mixed histology containing at least 10% carcinosarcoma, clear cell, or serous histology. [b]Patients were randomized based on either local or central MMR/MSI testing results. Central testing was used if 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. [c]Treatment ends after 3 years, PD, toxicity, withdrawal of consent, investigator's decision, or death, whichever occurs first. Continued treatment with dostarlimab or placebo beyond 3 years may be considered following discussion between the Sponsor and the Investigator. AUC, area under the plasma or serum concentration-time curve; BICR, blinded independent central review; DCR, disease control rate; DOR, duration of response, EC, endometrial cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; HRQOL, health-related quality of life; IHC, immunohistochemistry; INV, investigator assessment; MMR, mismatch repair; MSI, microsatellite instability; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PRO, patient-reported outcome; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Stratification Factors

Variable, n (%)	dMMR/MSI-H		Overall	
	Dostarlimab+CP (N=53)	Placebo+CP (N=65)	Dostarlimab + CP (N=245)	Placebo + CP (N=249)
MMR/MSI status				
dMMR/MSI-H	53 (100)	65 (100)	53 (21.6)	65 (26.1)
MMRp/MSS	—	—	192 (78.4)	184 (73.9)
Prior external pelvic radiation				
Yes	8 (15.1)	13 (20.0)	41 (16.7)	45 (18.1)
No	45 (84.9)	52 (80.0)	204 (83.3)	204 (81.9)
Disease status				
Primary stage III	10 (18.9)	14 (21.5)	45 (18.4)	47 (18.9)
Primary stage IV	16 (30.2)	19 (29.2)	83 (33.9)	83 (33.3)
Recurrent	27 (50.9)	32 (49.2)	117 (47.8)	119 (47.8)

CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; MMR, mismatch repair; MMRp, mismatch repair proficient; MSI, microsatellite instability; MSI-H, microsatellite instability-high; MSS, microsatellite stable.

Patient Population and Baseline Characteristics

	dMMR/MSI-H		Overall	
	Dostarlimab + CP (N=53)	Placebo + CP (N=65)	Dostarlimab + CP (N=245)	Placebo + CP (N=249)
Age				
Median age (range), y	61 (45–81)	66 (39–85)	64 (41–81)	65 (28–85)
≥65 y, n (%)	23 (43.4)	35 (53.8)	118 (48.2)	135 (54.2)
Race, n (%)				
White	44 (83.0)	56 (86.2)	189 (77.1)	191 (76.7)
Black	4 (7.5)	6 (9.2)	28 (11.4)	31 (12.4)
Asian	2 (3.8)	0	7 (2.9)	8 (3.2)
Other[a]	3 (5.7)	3 (4.6)	21 (8.6)	19 (7.6)
ECOG PS, n (%)[b]				
0	28 (53.8)	39 (60.0)	145 (60.2)	160 (65.0)
1	24 (46.2)	26 (40.0)	96 (39.8)	86 (35.0)
BMI				
Median BMI (range)	30.6 (20.1-54.4)	35.5 (17.9-58.1)	30.8 (17.6-60.6)	32.8 (17.7-68.0)
Measurable disease at baseline, n (%)				
Yes	49 (92.5)	58 (89.2)	212 (86.5)	219 (88.0)
No	4 (7.5)	7 (10.8)	33 (13.5)	30 (12.0)

	dMMR/MSI-H		Overall	
	Dostarlimab + CP (N=53)	Placebo + CP (N=65)	Dostarlimab + CP (N=245)	Placebo + CP (N=249)
Prior Anticancer Treatment, n (%)				
Yes	7 (13.2)	10 (15.4)	48 (19.6)	52 (20.9)
Prior Anticancer Surgery, n (%)				
Yes	49 (92.5)	60 (92.3)	224 (91.4)	224 (90.0)
Histology type, n (%)				
Carcinosarcoma	4 (7.5)	1 (1.5)	25 (10.2)	19 (7.6)
Endometrioid	44 (83.0)	56 (86.2)	134 (54.7)	136 (54.6)
Mixed carcinoma[c]	2 (3.8)	4 (6.2)	10 (4.1)	9 (3.6)
Serous adenocarcinoma	1 (1.9)	1 (1.5)	50 (20.4)	52 (20.9)
Clear cell adenocarcinoma	0	0	8 (3.3)	9 (3.6)
Mucinous adenocarcinoma	0	0	0	1 (0.4)
Undifferentiated carcinoma	0	0	1 (0.4)	2 (0.8)
Other	2 (3.8)	3 (4.6)	17 (6.9)	21 (8.4)

[a]Other includes patients identifying as American Indian or Alaska native, native Hawaiian or other Pacific Islander, unknown, or not reported. [b]Patients with ECOG PS: 52 dostarlimab+CP dMMR/MSI-H, 65 placebo+CP dMMR/MSI-H, 241 dostarlimab+CP overall, 246 placebo+CP overall. [c]Mixed carcinoma ≥10% of carcinosarcoma, clear cell, or serous histology.
BMI, body mass index; CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; MSI-H, microsatellite instability-high.

Patient Population and Baseline Characteristics

	dMMR/MSI-H		Overall	
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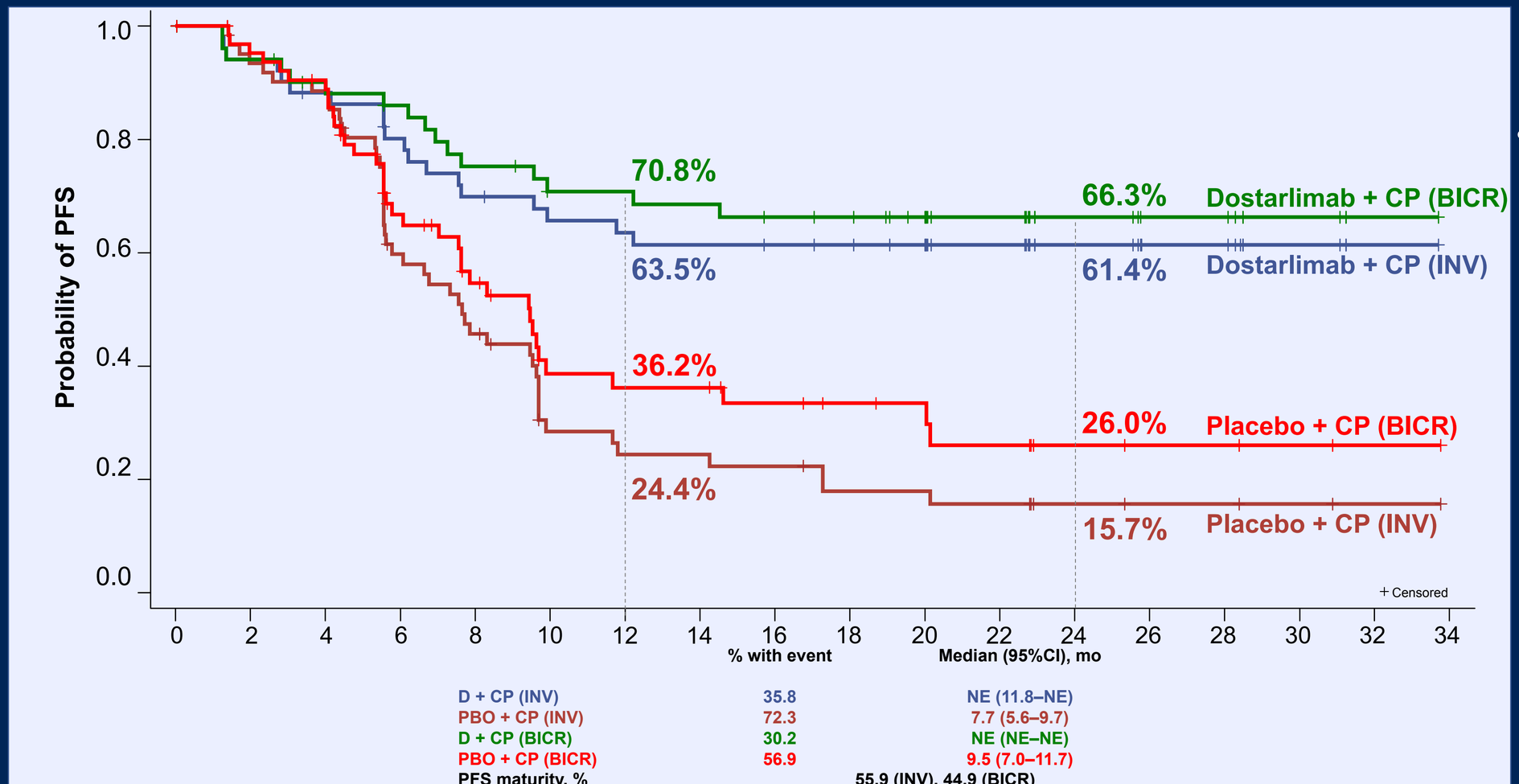
Mixed carcinoma[c]	2 (3.8)	4 (6.2)	10 (4.1)	9 (3.6)
Serous adenocarcinoma	1 (1.9)	1 (1.5)	50 (20.4)	52 (20.9)
Clear cell adenocarcinoma	0	0	8 (3.3)	9 (3.6)
Mucinous adenocarcinoma	0	0	0	1 (0.4)
Undifferentiated carcinoma	0	0	1 (0.4)	2 (0.8)
Other	2 (3.8)	3 (4.6)	17 (6.9)	21 (8.4)

[a]Other includes patients identifying as American Indian or Alaska native, native Hawaiian or other Pacific Islander, unknown, or not reported. [b]Patients with ECOG PS: 52 dostarlimab+CP dMMR/MSI-H, 65 placebo+CP dMMR/MSI-H, 241 dostarlimab+CP overall, 246 placebo+CP overall. [c]Mixed carcinoma ≥10% of carcinosarcoma, clear cell, or serous histology.
BMI, body mass index; CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; MSI-H, microsatellite instability-high.

dMMR/MSI-H Population



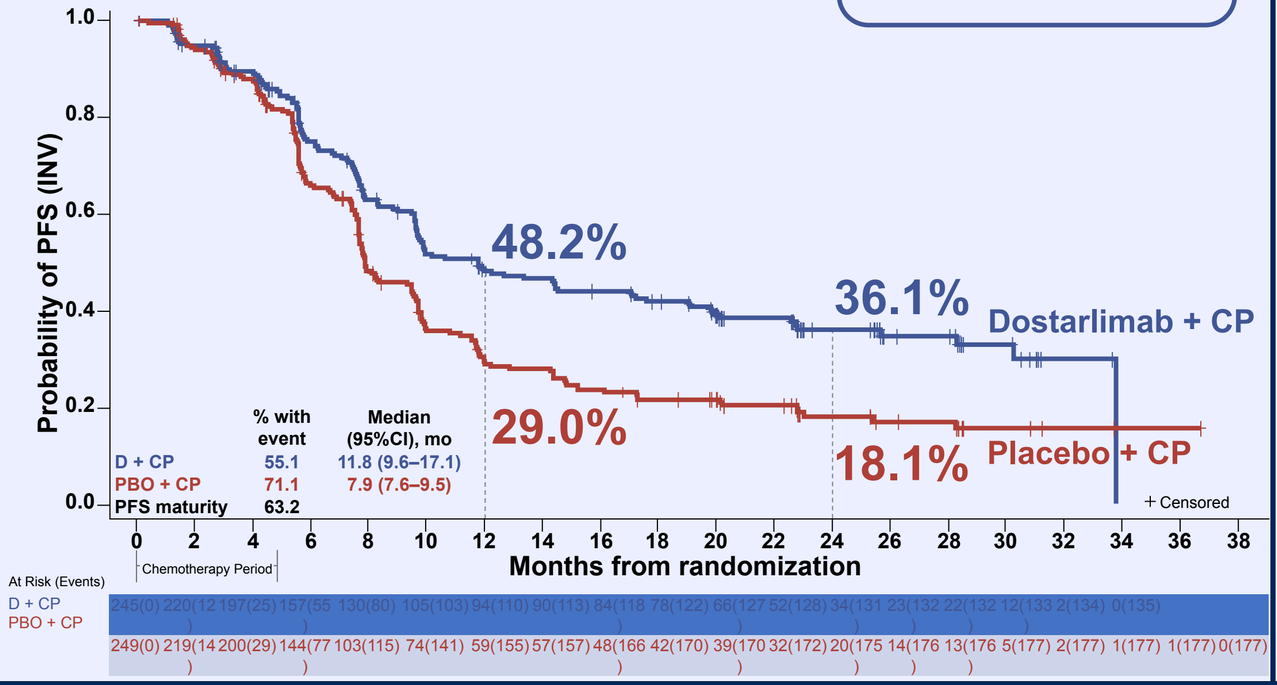
- Agreement on determination of event/censoring for PFS per INV and BICR was achieved for
  - Dostarlimab + CP 83.0%
  - Placebo + CP 78.5%

Agreement is on event/censoring only and does not include timing.
BICR, blinded independent central review; CP, carboplatin-paclitaxel; D, dostarlimab; dMMR, mismatch repair deficient; HR, hazard ratio; INV, investigator assessment; MSI-H, microsatellite instability-high; NE, not estimable; PBO, placebo; PFS, progression-free survival.

Overall Population

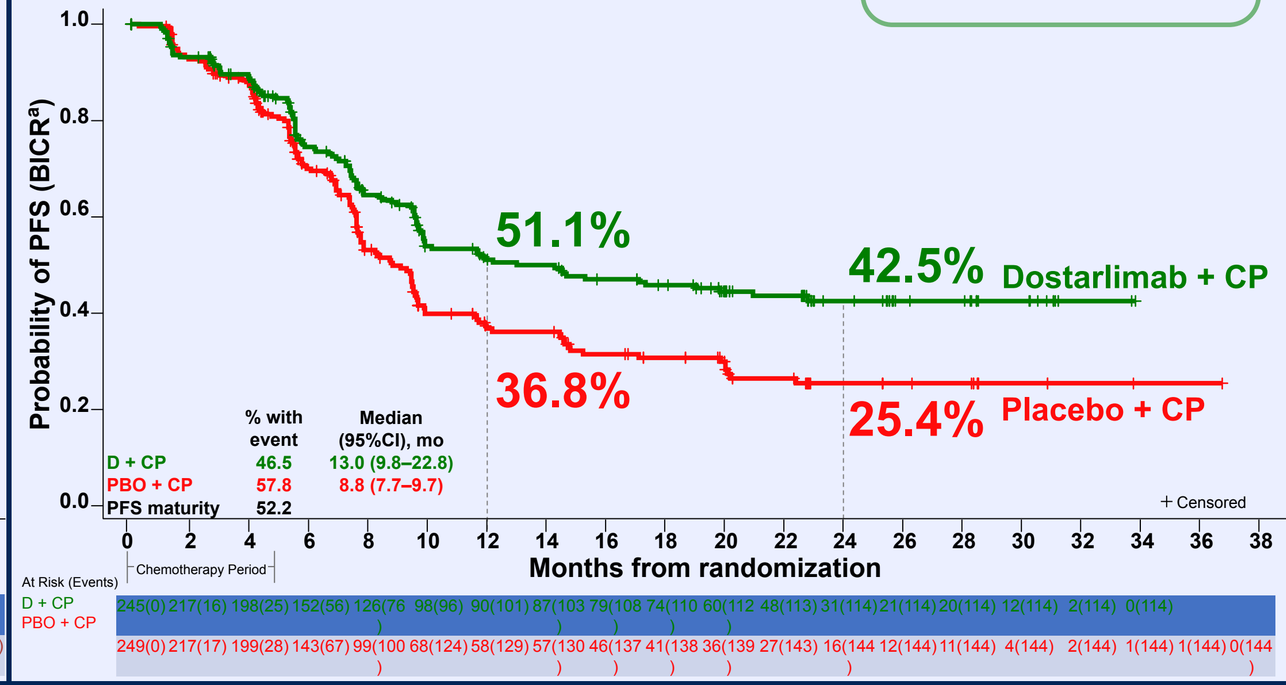
INV

HR, 0.64
(95% CI, 0.507–0.800)
***P*<0.0001**



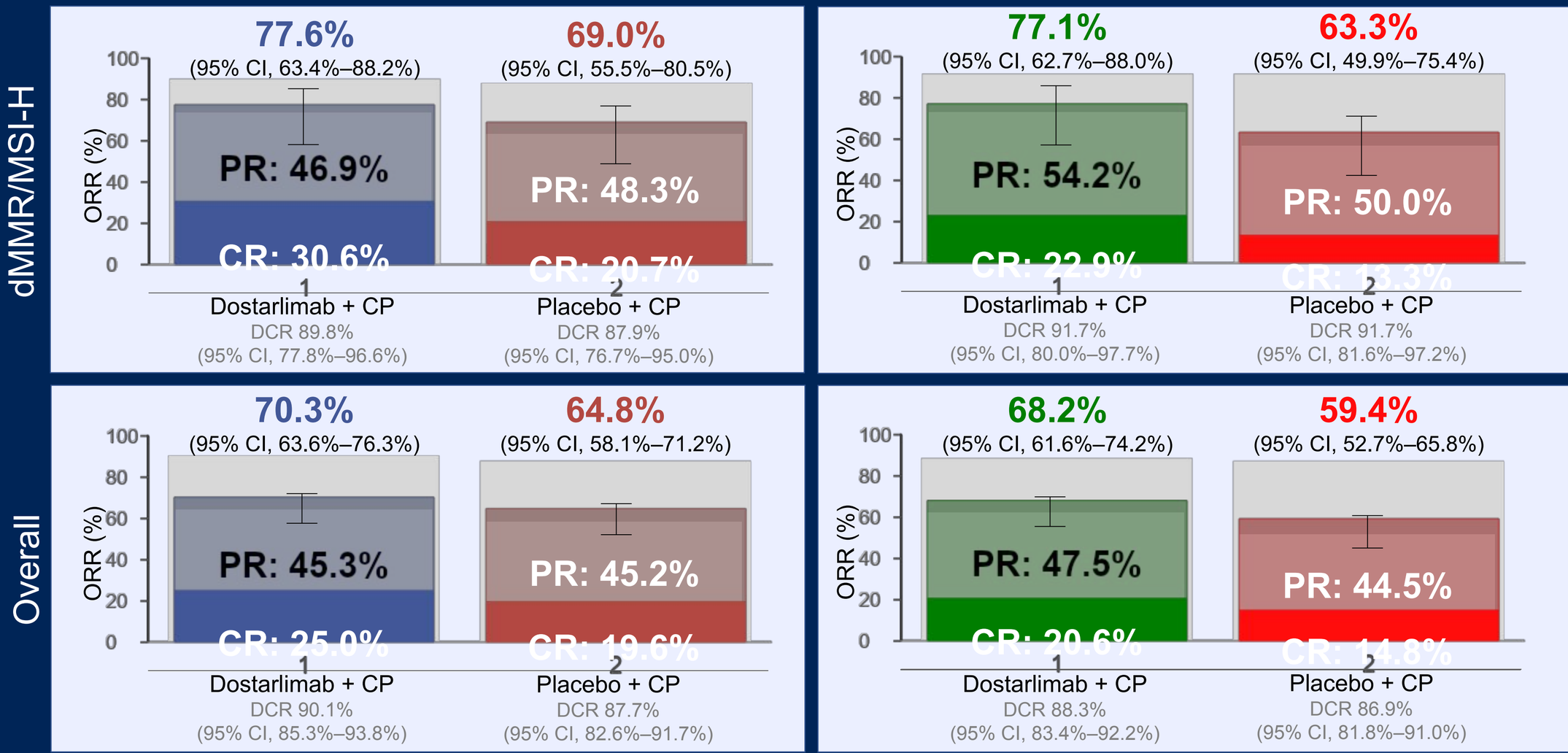
BICR

HR, 0.66
(95% CI, 0.517–0.853)
***P*<0.0006[a]**



[a]Nominal p-value.
From New England Journal of Medicine, Mirza MR, Chase DM, Slomovitz MD, et al, Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer. DOI: 10.1056/NEJMoa2216334. Copyright © 2023 Massachusetts Medical Society.
BICR, blinded independent central review; CP, carboplatin-paclitaxel; HR, hazard ratio; INV, investigator assessment; NE, not estimable; PFS, progression-free survival.

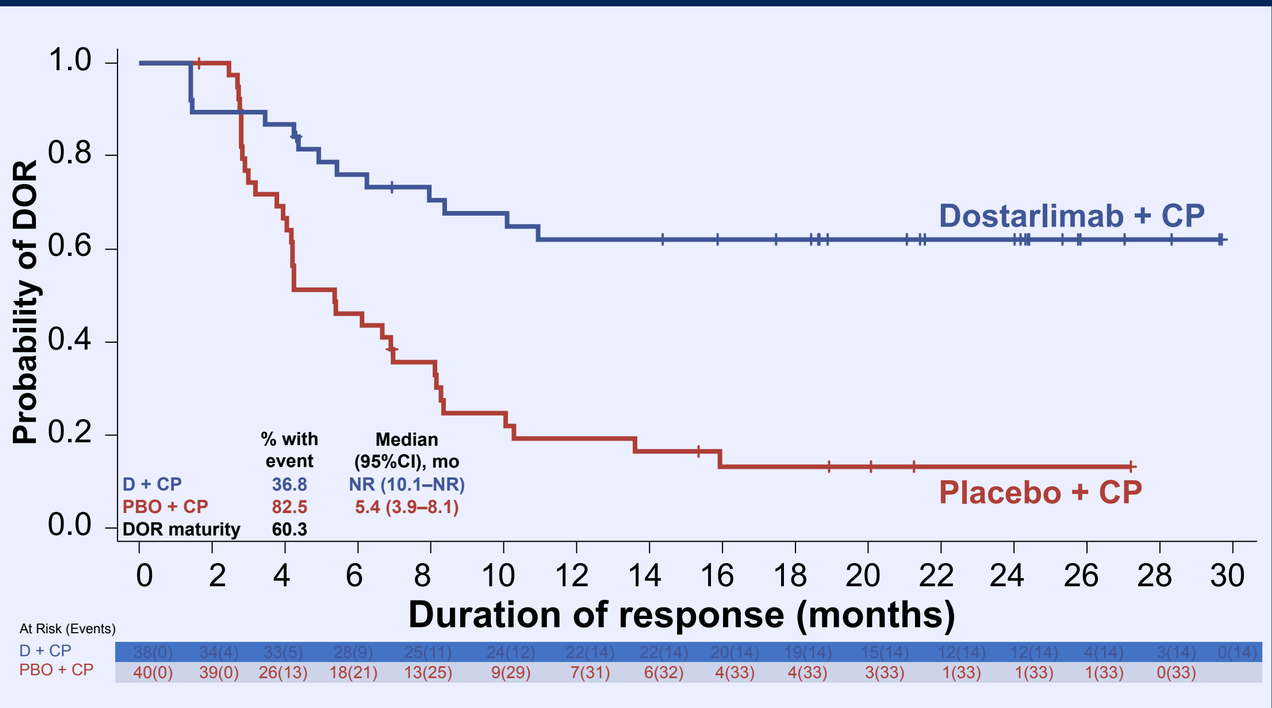
Consistent Objective Response Rate by INV and by BICR[a]



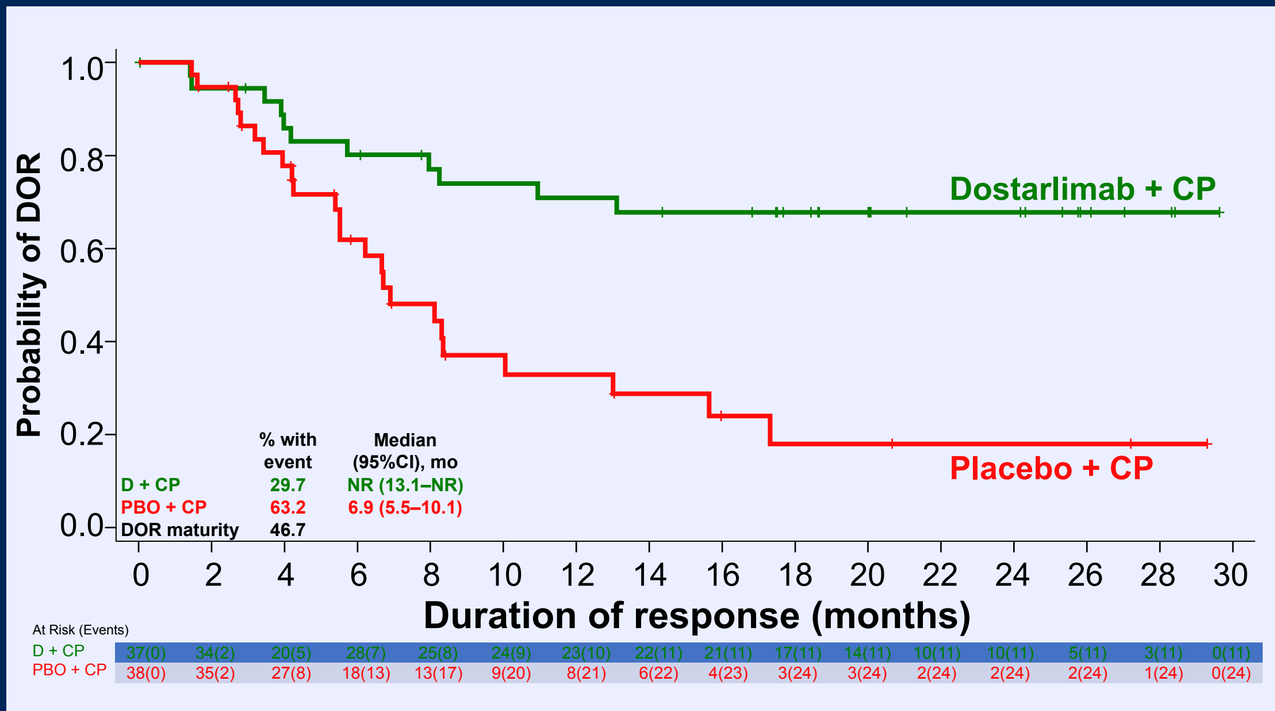
[a]Assessed in patients with evaluable disease at baseline. BICR, blinded independent central review; CP, carboplatin-paclitaxel; CR, complete response; DCR, disease control rate; dMMR, mismatch repair deficient; INV, investigator assessment; MSI-H, microsatellite instability-high; ORR, objective response rate; PR, partial response.

Dostarlimab+CP Led to More Durable Responses than CP Alone

INV



BICR



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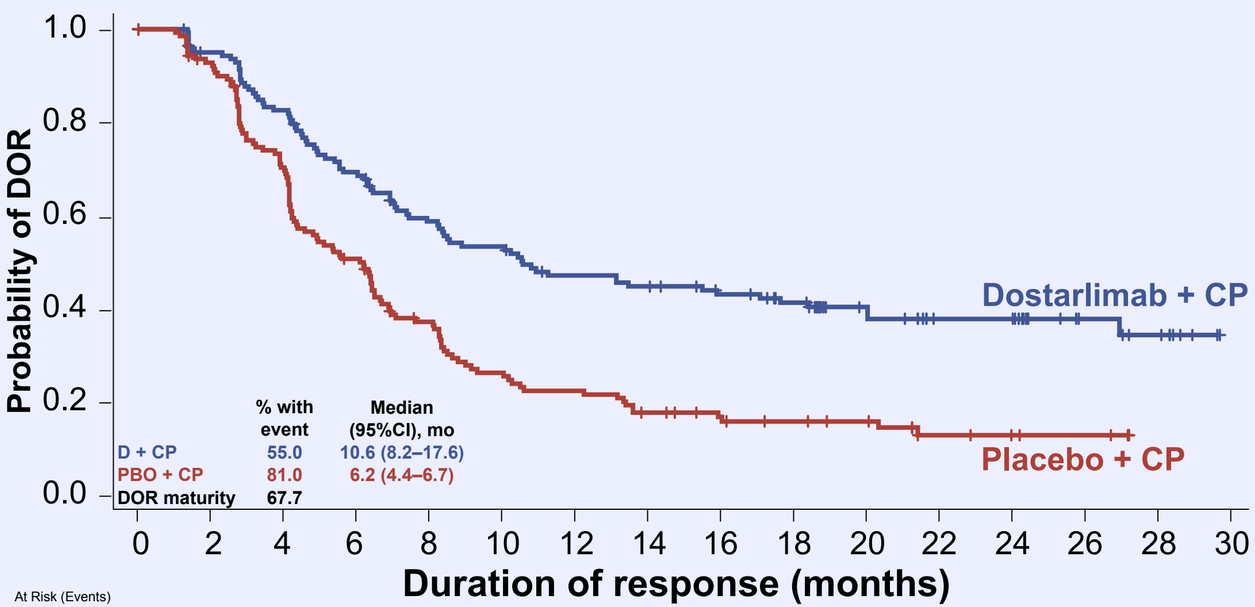
BICR, blinded independent central review; CP, carboplatin/paclitaxel; DOR, duration of response; INV, investigator assessment; NR, not reached.

Dostarlimab+CP Led to More Durable Responses than CP Alone

Consistent Duration of Response by INV and by BICR in Overall Population

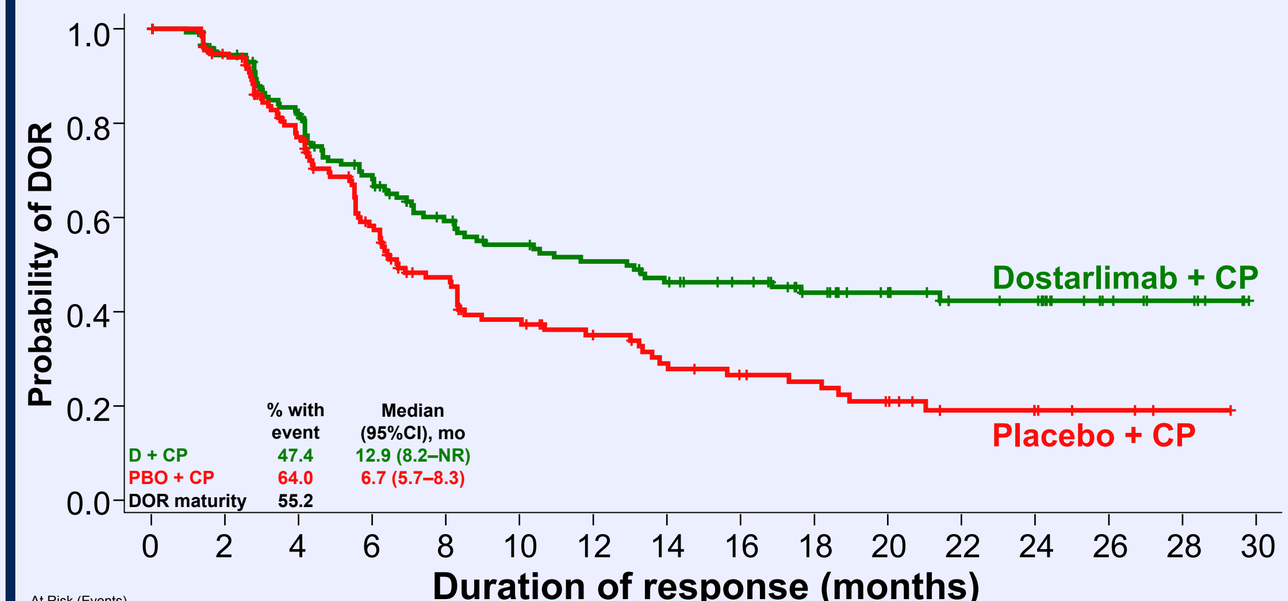
INV



At Risk (Events)

D + CP	149(0)	130(7)	113(24)	94(42)	77(56)	70(63)	60(71)	57(74)	51(76)	45(78)	32(79)	23(81)	23(81)	11(81)	8(82)	0(82)
PBO + CP	142 (0)	129(10)	97(41)	69(68)	48(86)	34(100)	29(105)	22(111)	18(112)	15(113)	13(113)	7(115)	5(115)	4(115)	0(115)	

BICR



At Risk (Events)

D + CP	152(0)	130(8)	110(25)	89(42)	71(54)	63(60)	58(64)	52(69)	47(69)	37(71)	30(71)	21(72)	20(72)	9(72)	6(72)	0(72)
PBO + CP	136(0)	122(7)	94(29)	66(51)	48(63)	37(72)	30(75)	24(80)	20(82)	18(83)	14(86)	8(87)	6(87)	4(87)	1(87)	0(87)

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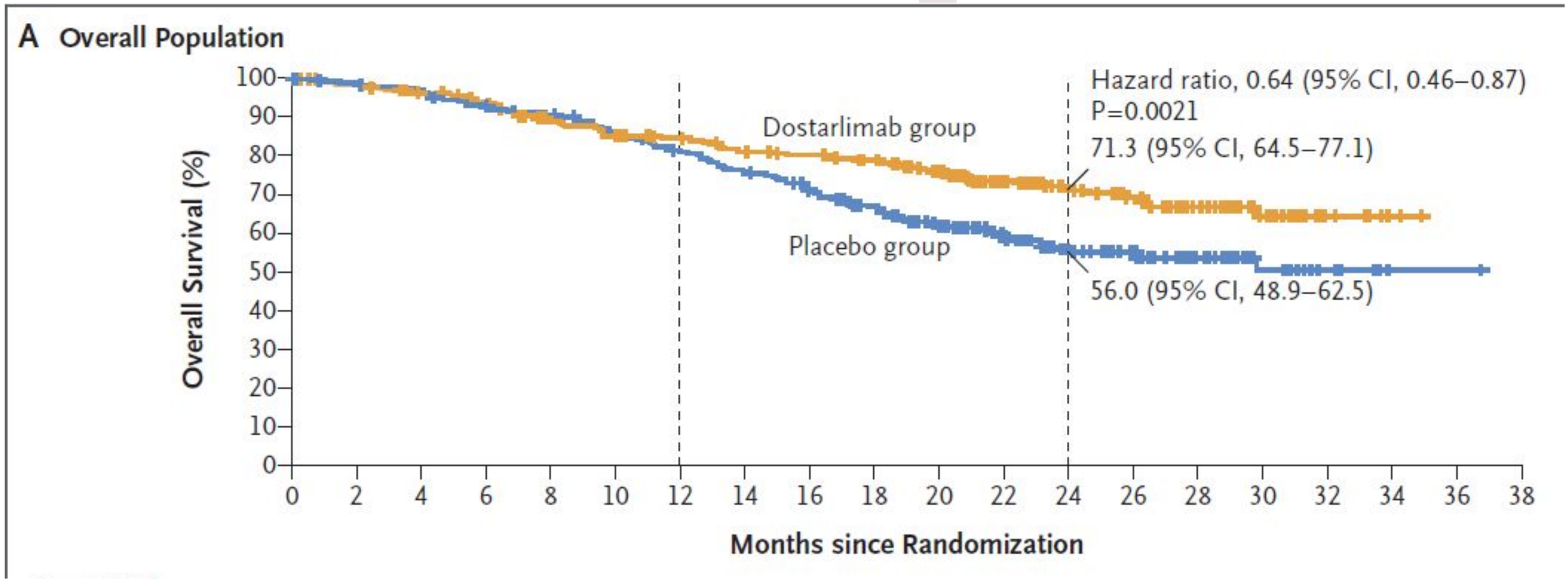
BICR, blinded independent central review; CP, carboplatin/paclitaxel; DOR, duration of response; INV, investigator assessment; NR, not reached.

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)

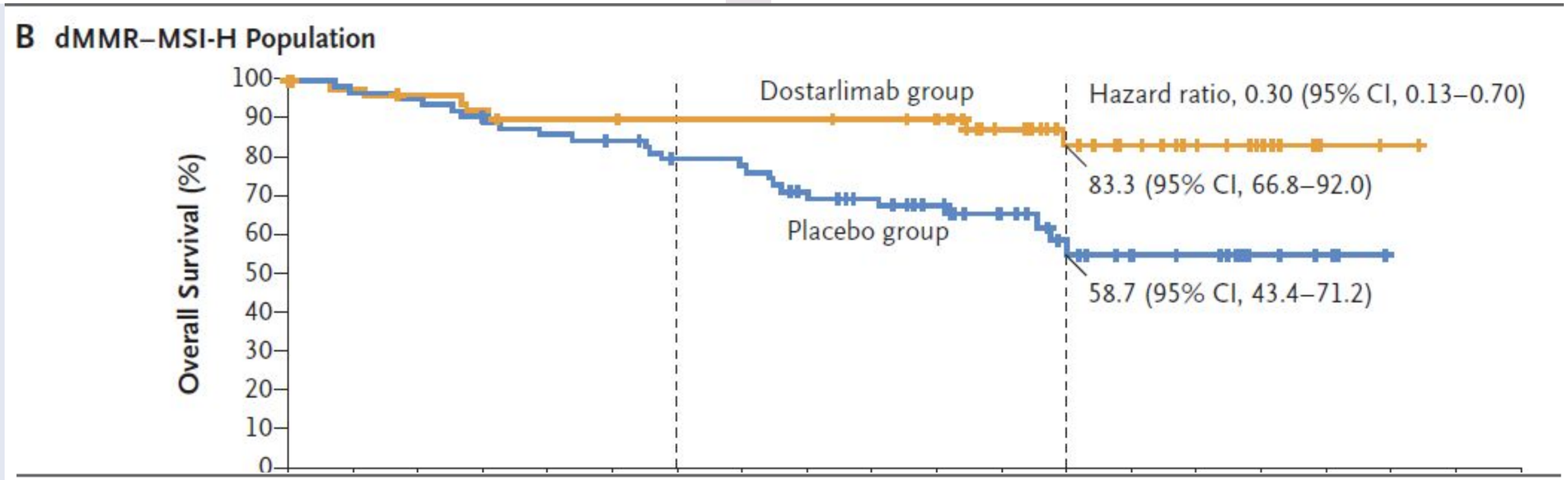
[a]3 deaths were not related to study treatment (opiate overdose, COVID-19, and general physical health deterioration). [b]One death was considered by the investigator as related to dostarlimab plus CP and occurred during the first 6 cycles (myelosuppression); one death was related to dostarlimab and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

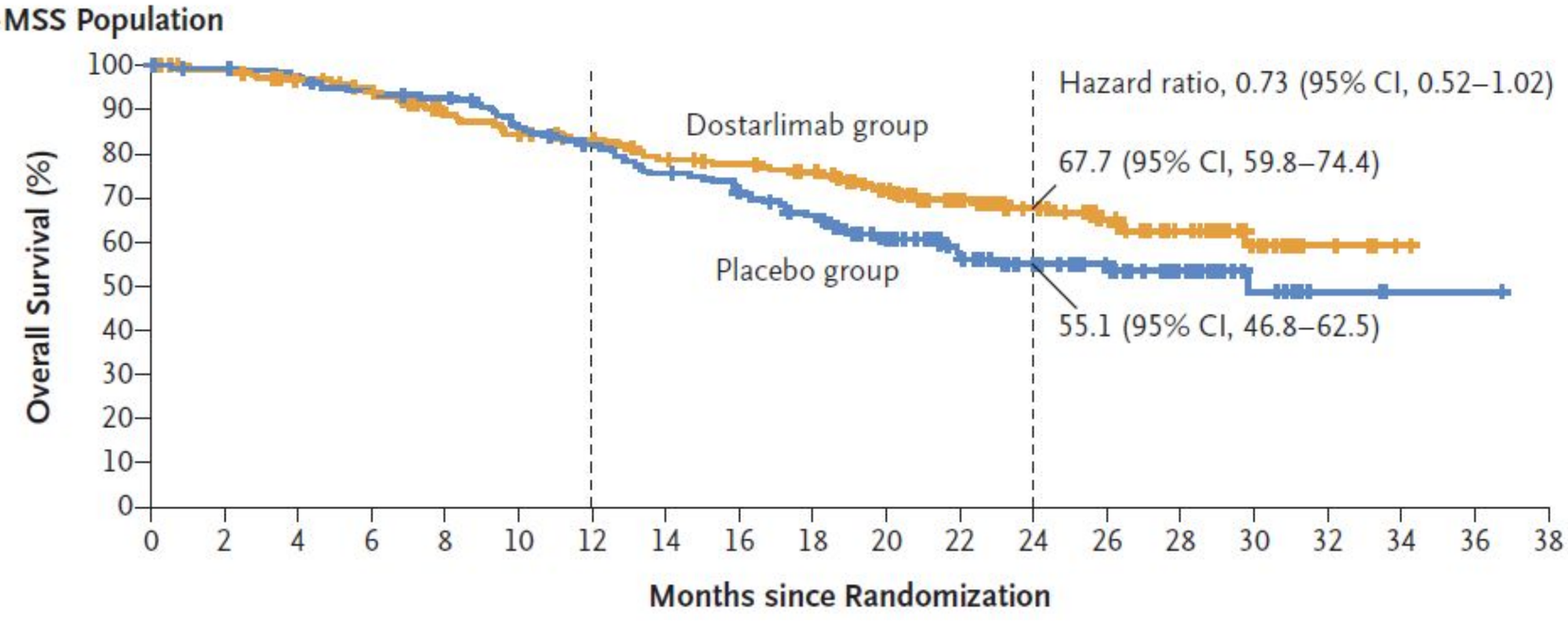
OVERALL SURVIVAL



Mirza MR, et al. N Engl J Med 2023; DOI: 10.1056/NEJMoa2216334

OVERALL SURVIVAL





Mirza MR, et al. N Engl J Med 2023; DOI: 10.1056/NEJMoa2216334

2023 ASCO ANNUAL MEETING

Hyperthermic intraperitoneal chemotherapy in ovarian cancer

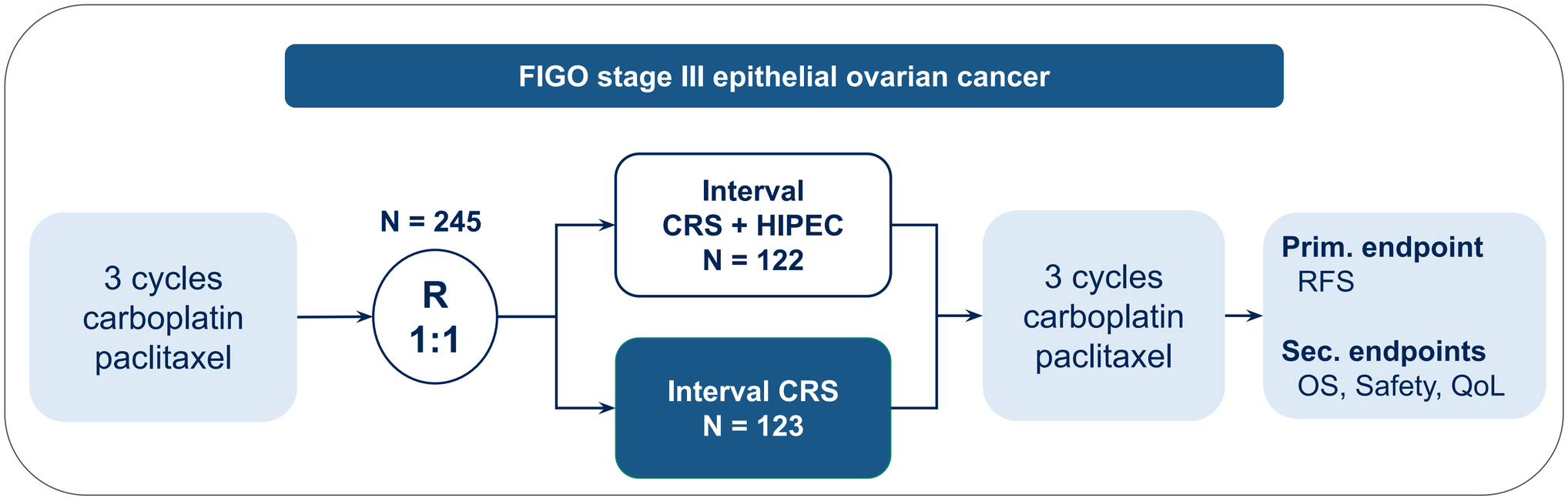
Final survival analysis of the phase III OVHIPEC-1 trial

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

Prof. Gabe S. Sonke, MD, PhD – contact: ovhipec@nki.nl

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

Prof. Gabe S. Sonke, MD, PhD – contact: ovhipec@nki.nl

Baseline characteristics

	CRS-HIPEC (N=122)	CRS (N=123)
Median age – yr (IQR)	61 (55–66)	63 (56–66)
WHO performance status – no. (%)		
0-1	87 (71)	86 (70)
2-3	6 (5)	5 (4)
unknown	29 (24)	32 (26)
Tumor histologic type – no. (%)		
High-grade serous	112 (92)	107 (87)
Other	10 (8)	16 (13)
Prior suboptimal surgery – no. (%)		
Yes	12 (10)	12 (10)
No	110 (90)	111 (90)
No of regions affected at start of interval CRS – no. (%)		
0-5	83 (68)	83 (67)
6-8	39 (32)	40 (33)
Homologous recombination deficiency – no. (%)*		
BRCAm	18 (17)	16 (17)
BRCAwt / HRD	35 (33)	30 (32)
BRCAwt / non-HRD	53 (50)	48 (51)

* BRCA/HRD for 200 patients; BRCA in germline and/or tumor

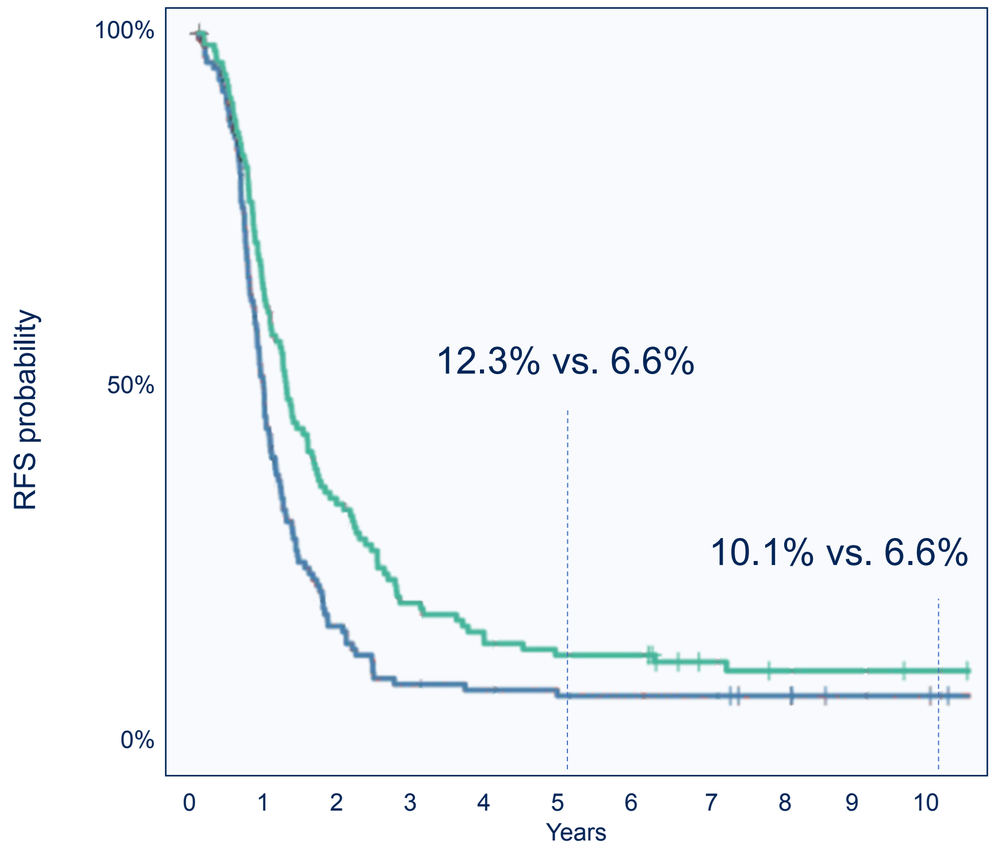
Prof. Gabe S. Sonke, MD, PhD – contact: ovhipec@nki.nl

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)

Prof. Gabe S. Sonke, MD, PhD – contact: ovhipec@nki.nl

RFS after ten years follow-up

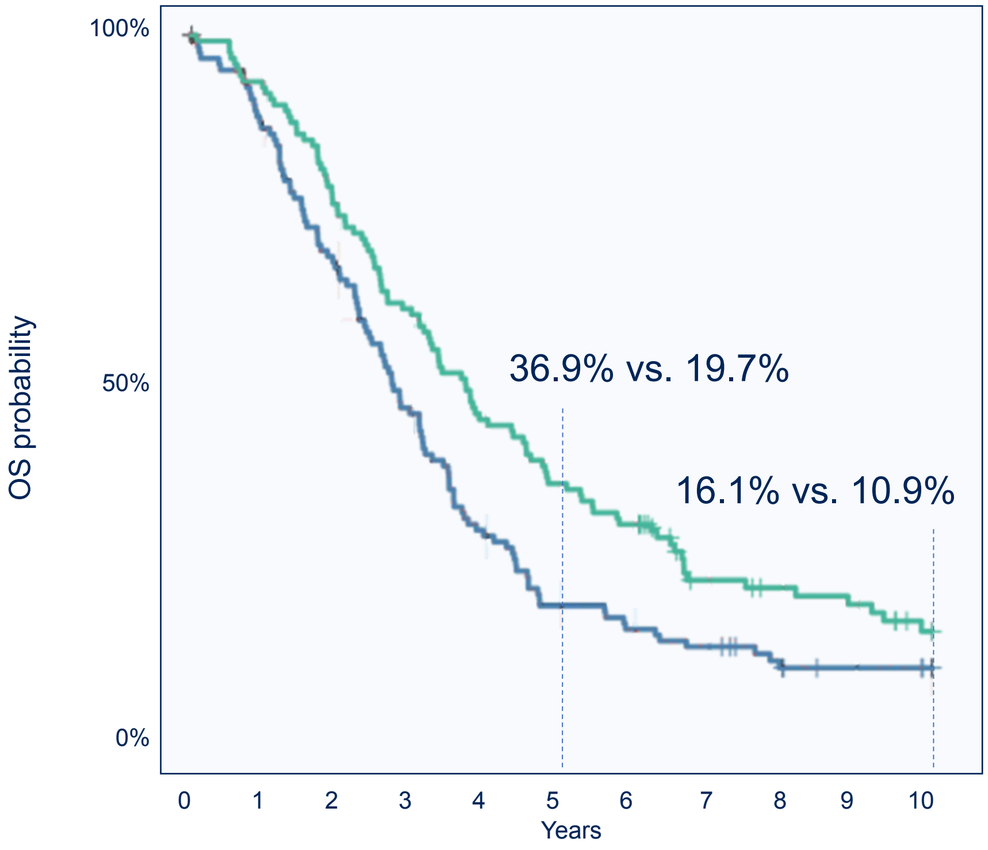


	CRS-HIPEC	CRS
Median RFS, mo	14.3	10.7
HR (95%CI)	**0.63 (0.48 – 0.83)**	
Stratified log-rank p	0.0008	

HIPEC delays recurrences

Prof. Gabe S. Sonke, MD, PhD – contact: ovhipec@nki.nl

OS after ten years follow-up



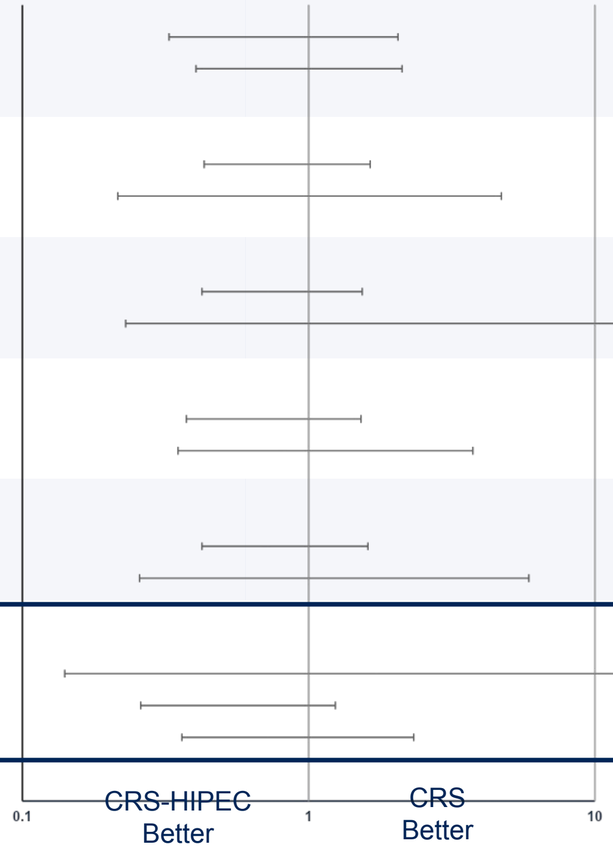
	CRS-HIPEC	CRS
Median OS, mo	44.9	33.3
HR (95%CI)	**0.70 (0.53 – 0.92)**	
Stratified log-rank p	0.0113	

HIPEC improves long-term overall survival

Prof. Gabe S. Sonke, MD, PhD – contact: ovhipec@nki.nl

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					0.0159
BRCAm	12/18	15/16	1.73	(0.64-4.72)	
HRD / BRCAwt	34/35	23/30	0.43	(0.21-0.89)	
Non-HRD / BRCAwt	49/53	43/48	0.72	(0.42-1.23)	



HRD/BRCAwt group may derive most benefit
This finding warrants further evaluation

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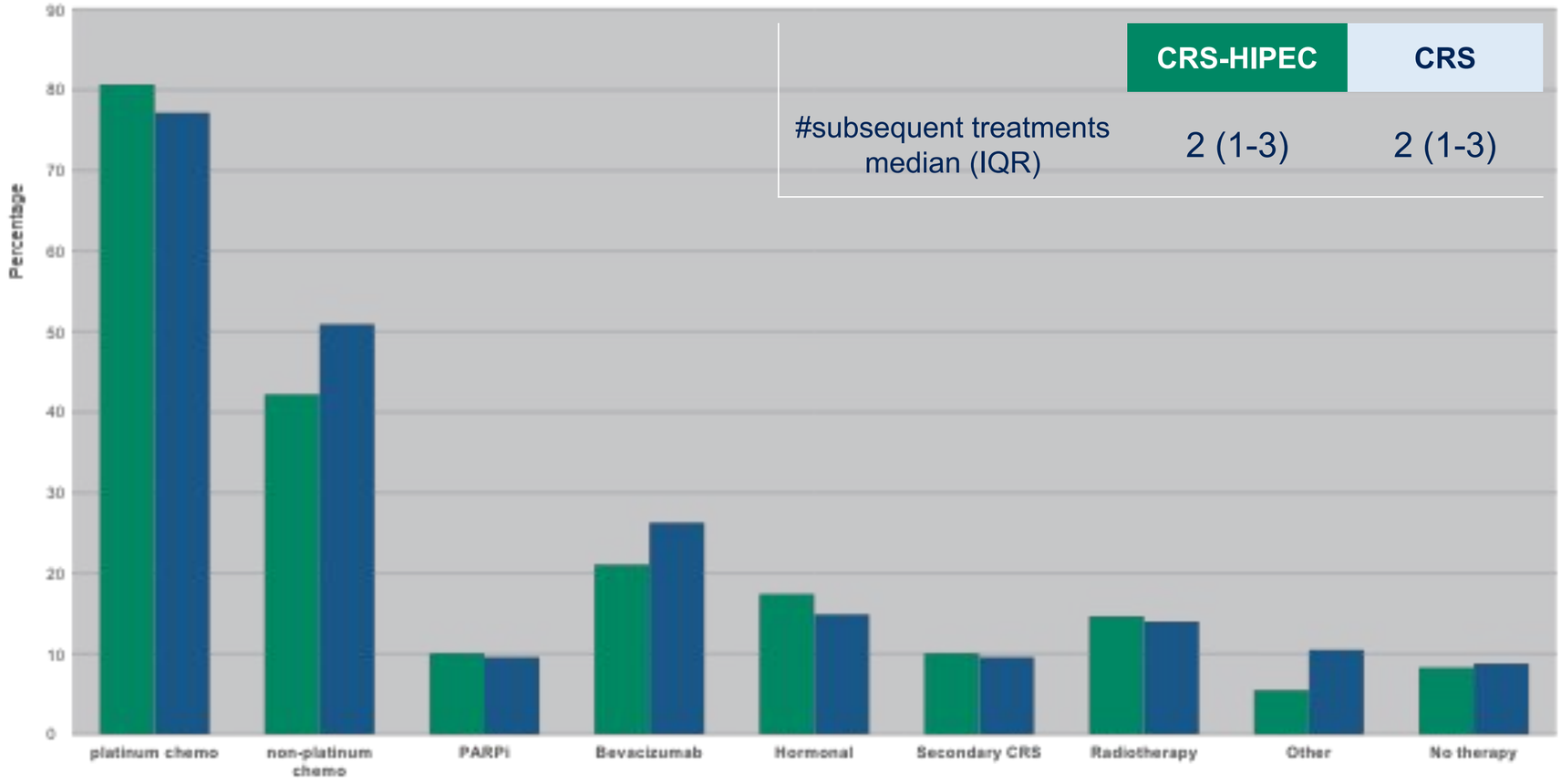
1. Koole et al, Int J Cancer, 2022

Treatment for recurrent disease

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



No significant difference in therapies for recurrences

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Conclusion / Take-Away

10-year survival update from OVHIPEC-1 confirms benefit of HIPEC
in patients with stage III ovarian cancer undergoing interval CRS

HIPEC added to interval CRS

Delays recurrences
Improves overall survival
Does not impact subsequent therapy

Prof. Gabe S. Sonke, MD, PhD – contact: ovhipec@nki.nl

2023 ASCO ANNUAL MEETING

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

Less radical surgery

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Review

Conservative management of early stage cervical cancer: Is there a role for less radical surgery?

Kathleen M. Schmeler *, Michael Frumovitz, Pedro T. Ramirez

Department of Gynecologic Oncology, The University of Texas M.D. Anderson Cancer Center, 1155 Herman Pressler Drive, Houston, TX 77030, USA

Author	Year	Low-risk criteria	N	Parametrial involvement in low-risk group (%)
Kinney [13]	1995	Squamous histology only, tumor <2 cm, no LVSI*	83	0.0%
Covens [14]	2002	All histologies, tumor <2 cm, DOI** <10 mm, negative pelvic lymph nodes	536	0.6%
Stegeman [15]	2007	Squamous, adenocarcinoma, adenosquamous or clear cell histology, tumor <2 cm, DOI** <10 mm, no LVSI*, negative pelvic lymph nodes	103	0.0%
Wright [16]	2008	All histologies, tumor <2 cm, no LVSI*, negative pelvic lymph nodes	270	0.4%
Frumovitz [19]	2009	Squamous, adenocarcinoma or adenosquamous histology, tumor <2 cm, no LVSI*	125	0.0%

*LVSI: lymphvascular space involvement
**DOI: depth of invasion

All retrospective data

N=1117 < 1%

Schmeler K et al. Gynecol Oncol 120:321, 2011

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*

Pelvic recurrence rate at 3 years

*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.

CX.5 Endpoints

Primary Endpoints

- **Pelvic recurrence rate at 3 years (PRR3)**

Secondary Endpoints

- Pelvic relapse free survival (PRFS)
- Extra pelvic relapse free survival (EPRFS)
- Relapse free survival (RFS)
- Overall Survival (OS)
- Rates of sentinel node detection, parametrial involvement, involved surgical margins, positive pelvic nodes
- Patient reported outcomes

700 randomized between December 2012 and November 2019

12 countries
130 centers

350 to **simple** hysterectomy and in intention to treat (ITT) population

350 to **radical** hysterectomy and in intention to treat (ITT) population

7 never received surgery

7 received radical hysterectomy

2 received simple hysterectomy

11 never received surgery

338 in treated population

344 in treated population

21 excluded at randomization or with post surgical findings of more extensive disease

317 in per protocol (PP) population

312 in per protocol (PP) population

32 excluded at randomization or with post surgical findings of more extensive disease

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)

Key Baseline Patient Characteristics

Characteristics	Simple Hysterectomy N=350 (%)	Radical Hysterectomy N=350 (%)	Total N=700
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)

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

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

All Treated Patients Post Surgery

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	

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)

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)
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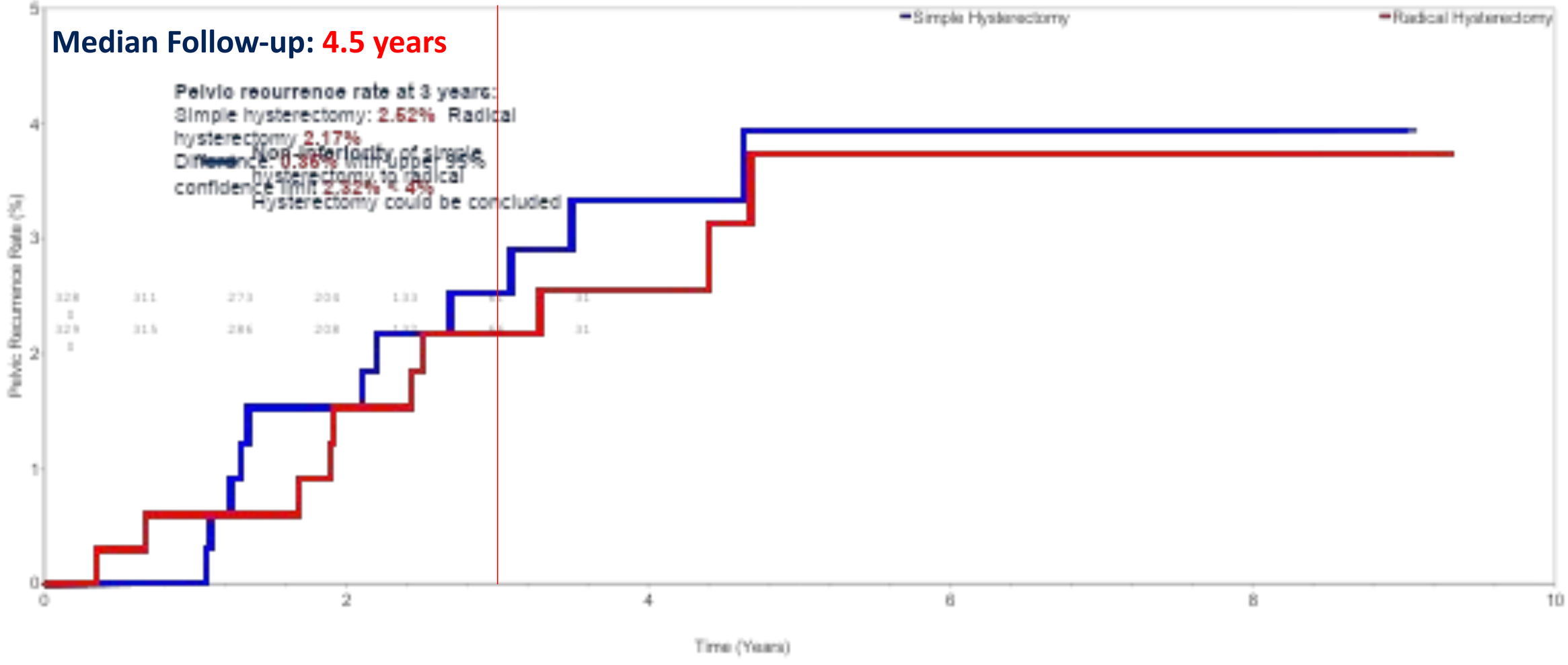
Extra pelvic only recurrences	4 (1.1)	0	4 (0.6)
Pelvic or extra pelvic recurrences	15 (4.3)	10 (2.9)	25 (3.6)

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)

Pelvic Recurrence Rate (ITT)

Median Follow-up: 4.5 years



PRESENTED BY: Marie Plante-SHAPE

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

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

Quality of Life and Sexual Health

Significant differences were seen between the 2 groups over time and **all were in favor of the simple hysterectomy group**

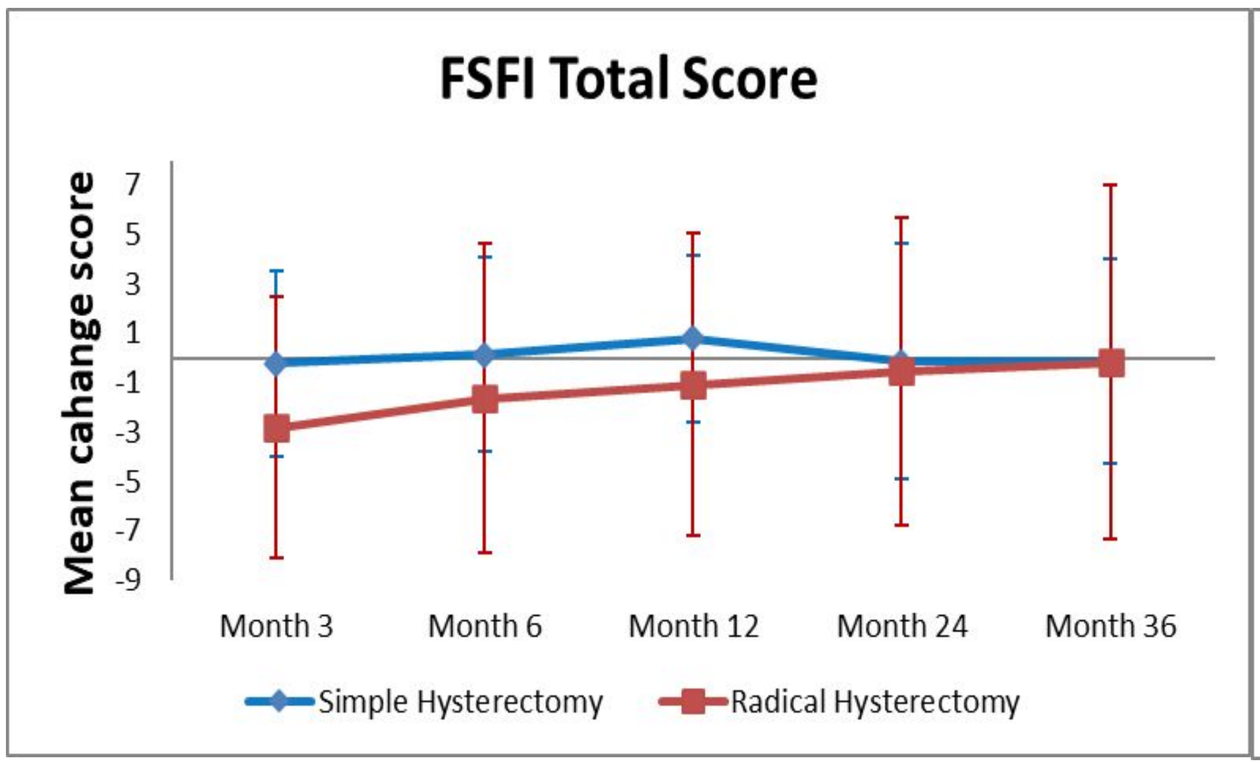
*From linear mixed models for change scores from baseline over time

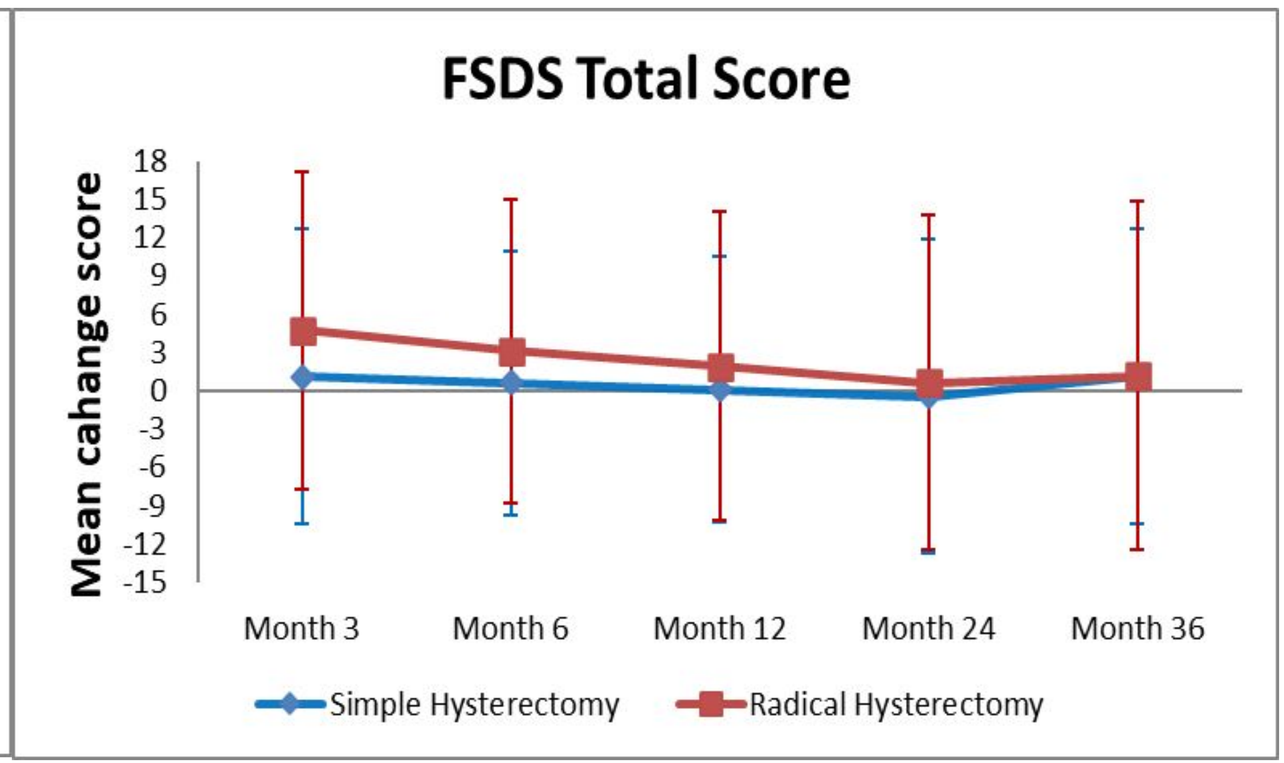
Scale	Effect Estimate*	P-value
EORTC QLQ-C30 pain scale	-4.53	p=0.02
EORTC QLQ-CX24		
•Symptom experiences	-2.12	p=0.02
•Body Image	-5.22	p=0.02
•Sexual Worry	-6.67	p=0.04
•Sexual Activities	-7.59	p=0.003
•Sexual Enjoyment	-7.67	p=0.049
FSFI Desire	0.37	p=0.002
FSFI Arousal	0.38	p=0.003
FSFI Lubrication	0.36	p=0.008
FSFI Total Score	1.82	p=0.006
FSDS Total Score	-2.47	p=0.02

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

Quality of Life and Sexual Health





Higher score indicating a **better level of sexual function**

Higher score indicating a **greater level of sexual-related distress**

Conclusion

- In early-stage low-risk cervical cancer, pelvic recurrence rate at three years with **simple hysterectomy** was **not inferior** to radical hysterectomy
- Fewer urological surgical complications following **simple hysterectomy**
- Better quality of life and sexual health measures were seen following **simple hysterectomy**
- Following adequate / rigorous preoperative assessment, **simple hysterectomy** can now be considered the **new standard of care** for patients with low-risk early-stage cervical cancer, supporting the concept of **surgical de-escalation** in those patients
  - Stage IA2-IB1 ≤ 2cm
  - < 10 mm depth of stromal invasion (LEEP/cone)
  - < 50% depth of stromal invasion (preop MRI)

2023 ASCO ANNUAL MEETING

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

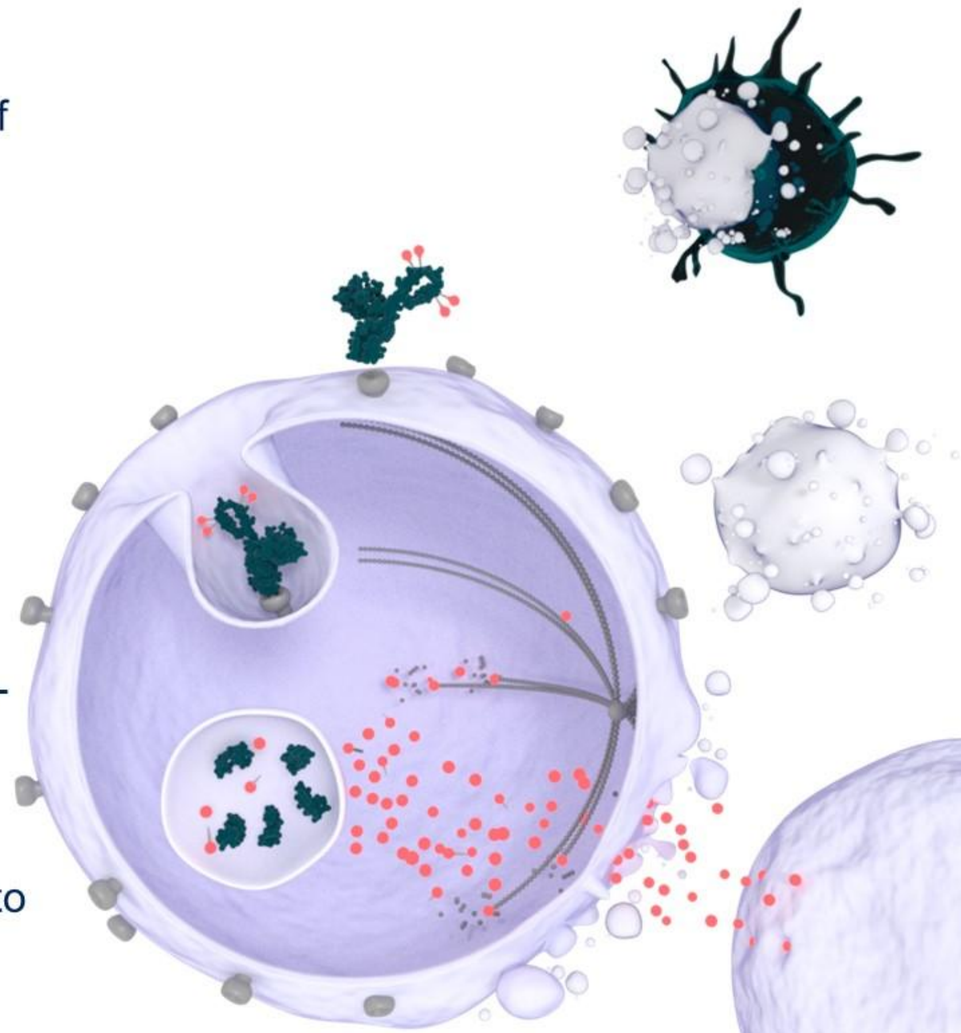
ENGOT European Network of Gynaecological Oncological Trial groups

GOG FOUNDATION® Transforming the standard of care™

PRESENTED BY: Kathleen Moore, Associate Director of Clinical Research, Stephenson Cancer Center University of Oklahoma College of Medicine

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



PFS, progression-free survival; OS, overall survival; FRα, folate receptor alpha; ORR, objective response rate; ADC, antibody-drug conjugate; mDOR, median duration of response; FDA, Food and Drug Administration; BEV, bevacizumab; US, United States; EU, Europe.

1. Pujade-Lauraine et al. *J Clin Oncol*. 2014;32(13):1302-1308. **2.** Richardson et al. *JAMA Oncol*. 2023;10.1001/jamaoncol.2023.0197. **3.** Moore et al. *Cancer*. 2017;123(16):3080-3087. **4.** Ab et al. *Mol Cancer Ther*. 2015;14(7):1605-1613. **5.** Markert et al. *Anticancer Res*. 2008;28(6A):3567-3572. **6.** Martin et al. *Gynecol Oncol*. 2017;147(2):402-407. 7. Data on file. **8.** Matulonis et al. *J Clin Oncol*. 2023:41(13):2436-2445. **9.** U.S. FOOD & DRUG ADMINISTRATION. BLA ACCELERATED APPROVAL. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/761310Orig1s000ltr.pdf. Accessed May 23, 2023.

PRESENTED BY: Kathleen Moore, Associate Director of Clinical Research, Stephenson Cancer Center University of Oklahoma College of Medicine

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

AIBW, adjusted ideal body weight; BEV; bevacizumab; BICR, blinded independent central review; BRCA, BReast CAncer gene; CA-125, cancer antigen 125; chemo, chemotherapy; DOR, duration of response; FRα, folate receptor alpha; IC, investigator's choice; IHC, immunohistochemistry; INV, investigator; MIRV, mirvetuximab soravtansine; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitors; PFI, platinum-free interval; PFS, progression-free survival; PFS2, time from randomization until second disease progression; PLD, pegylated liposomal doxorubicin; PROs, patient-reported outcomes; PS2+, positive staining intensity ≥2; Q3W, every 3 weeks.
[a]PROs will be measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, 28-item Ovarian Cancer Module (OV28) study instrument.
[b]Gynecological Cancer InterGroup (GCIG) criteria.

1. ClinicalTrials.gov identifier: NCT04209855. Updated June 16, 2022. Accessed October 5, 2022. https://clinicaltrials.gov/ct2/show/NCT04209855
2. Moore K, et al. Presented at: 2020 American Society of Clinical Oncology Annual Meeting; May 29-31, 2020; Virtual. Abstract TPS6103.

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Baseline Demographics and Stratification Factors (N=453)

Characteristics		MIRV (n=227)	IC Chemo (n=226)
Age, median (range)	Age in years	63 (32-88)	62 (29-87)
Stage at initial diagnosis, n (%)[a]	I-II III IV	9 (4) 137 (60) 76 (33)	9 (4) 147 (65) 65 (29)
BRCA mutation, n (%)	Yes No/Unknown	29 (13) 198 (87)	36 (16) 190 (84)
Prior exposure, n (%)	Bevacizumab PARPi Taxanes	138 (61) 124 (55) 227 (100)	143 (63) 127 (56) 224 (99)
Primary platinum-free interval, n (%)[b]	≤ 12 months > 12 months	146 (64) 80 (35)	142 (63) 84 (37)
Platinum-free interval, n (%)[c]	≤ 3 months > 3 - ≤6 months	88 (39) 138 (61)	99 (44) 124 (55)
Stratification Factor **No. of prior systemic therapies, n (%)**	1 2 3	31 (14) 91 (40) 105 (46)	32 (14) 91 (40) 103 (46)
Stratification Factor **Investigator Choice of Chemotherapy**	Paclitaxel PLD Topotecan	93 (41) 82 (36) 52 (23)	92 (41) 81 (36) 53 (23)

Data cutoff: March 6, 2023. **14% of patients remain on MIRV; 3% remain on IC Chemo**
BRCA, BReast CAncer gene; PARPi, poly (ADP-ribose) polymerase inhibitors; MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; PLD, pegylated liposomal doxorubicin,.
[a]Five patients (2%) in the MIRV arm and five patients in the IC chemo arm (2%) were missing information for stage at initial diagnosis. [b]One patient (<1%) in the MIRV arm was missing information on primary platinum-free interval.
[c]One patient (<1%) in the MIRV arm and 3 patients (1%) in the IC chemo arm enrolled with platinum-free interval of >6 months

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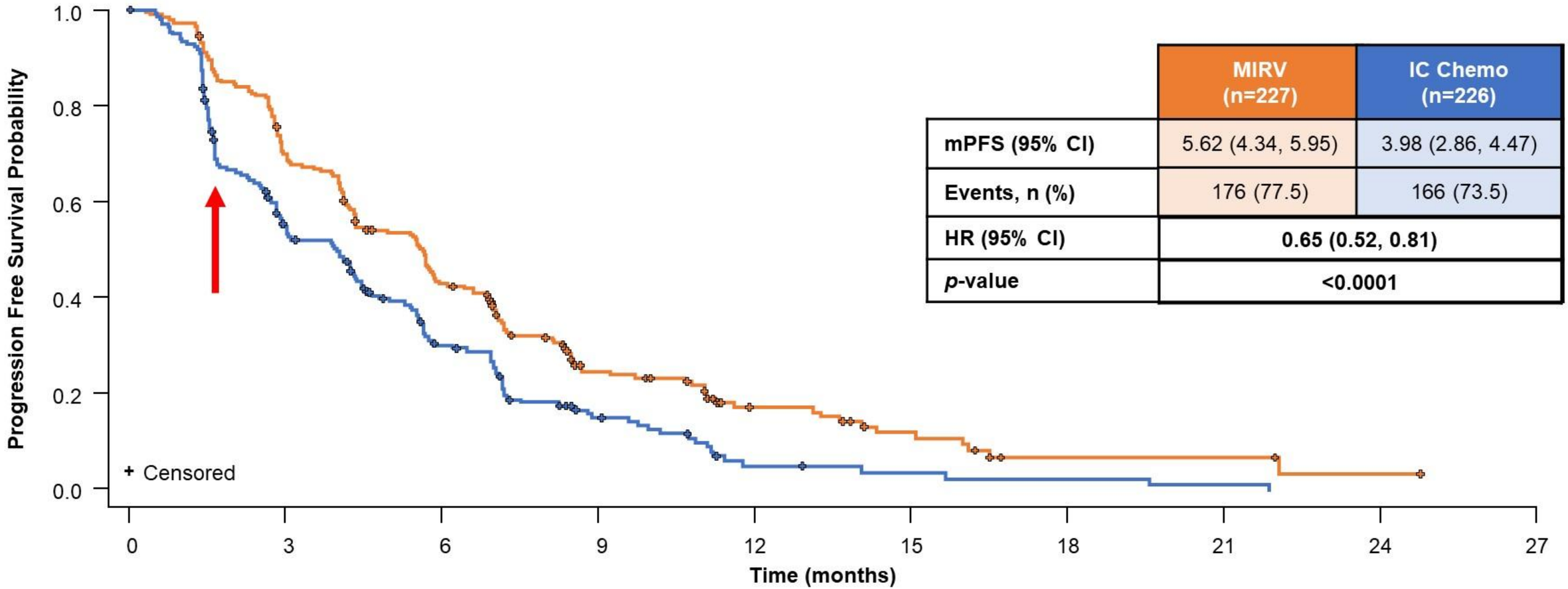
Primary Endpoint: Progression-Free Survival by Investigator



	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	

Data cutoff: March 6, 2023

MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mPFS, median progression-free survival; CI, confidence interval; HR, hazard ratio.

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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**

Data cutoff: March 6, 2023
MIRV, mirvetuximab soravtansine; IC chemo, investigator's choice chemotherapy; ORR, objective response rate; CI, confidence interval; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; OR, odds ratio.

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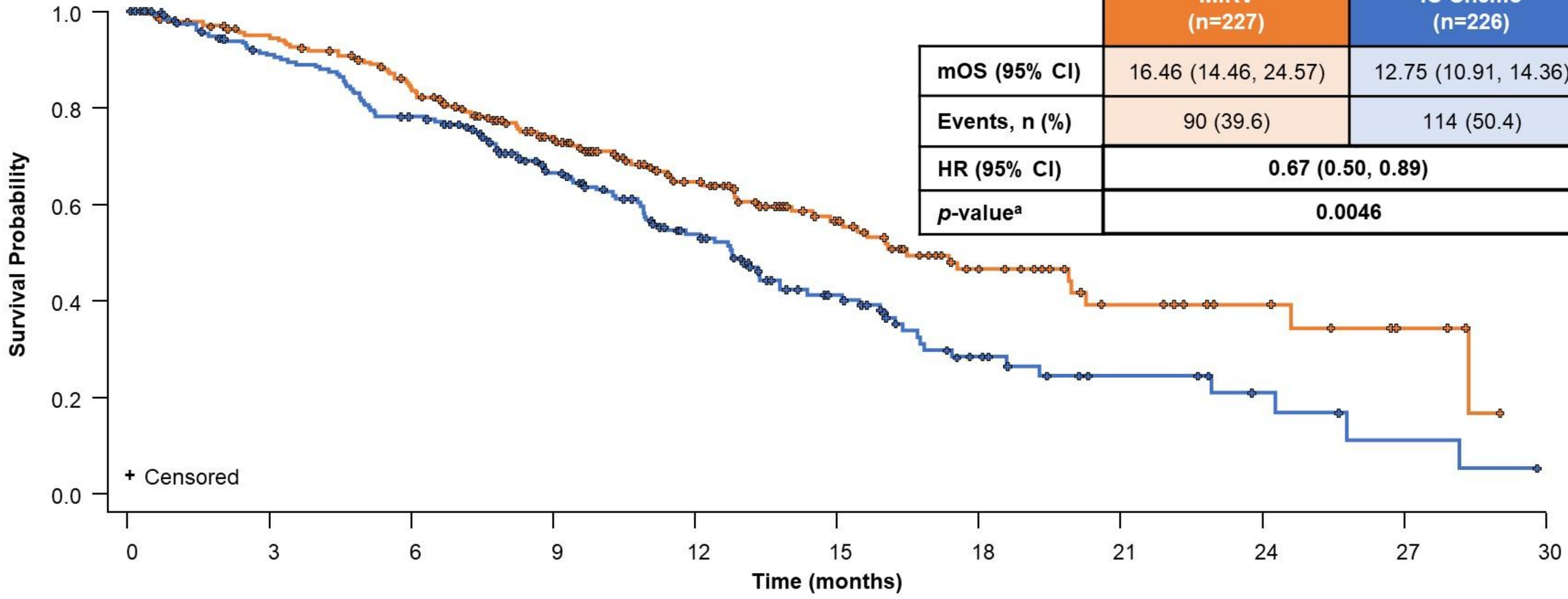
Overall Survival

	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

Data cutoff: March 6, 2023; median follow-up time: 13.11 months

MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mOS, median overall survival; CI, confidence interval; HR, hazard ratio.

[a]Overall survival is statistically significant based on pre-specified boundary p-value at interim analysis = 0.01313

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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)

Data cutoff: March 6, 2023
The safety population comprises all patients who received at least one dose of MIRV or IC Chemo
TEAEs, treatment-emergent adverse events; SAEs, serious adverse events; MIRV, mirvetuximab soravtansine; IC, investigator's choice chemotherapy.

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Summary

Recent advances reported in the 3 major pelvic malignancies in women.

Issues remain:

-Equity in access to innovative treatment

-Safety of minimally invasive surgeries for cervical cancer

-Enrollment of a more diverse population

-Statistical versus clinical significance

+

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