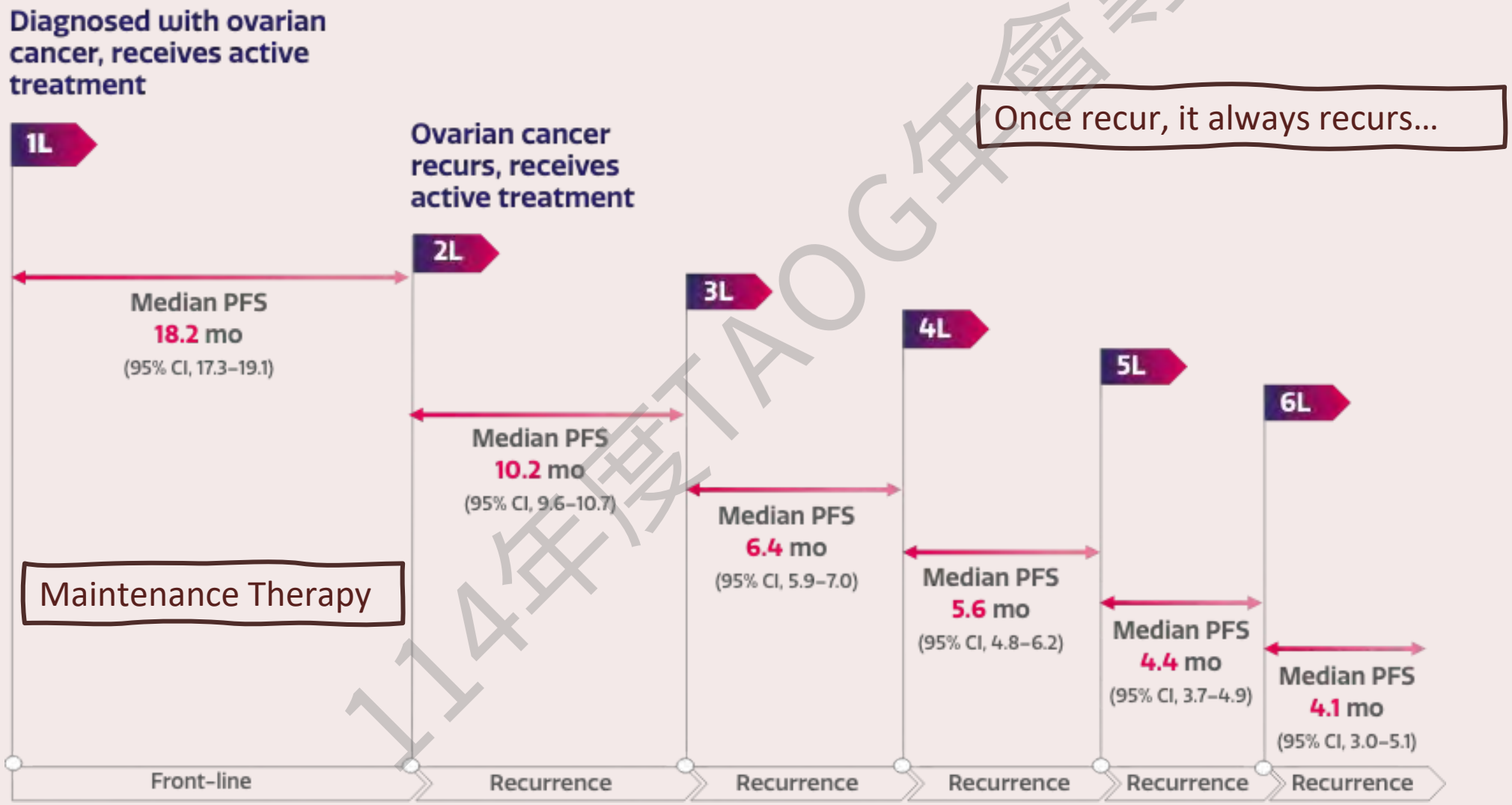
卵巢癌診斷與治療的新契機

馬偕紀念醫院 婦癌科

林玟瑄

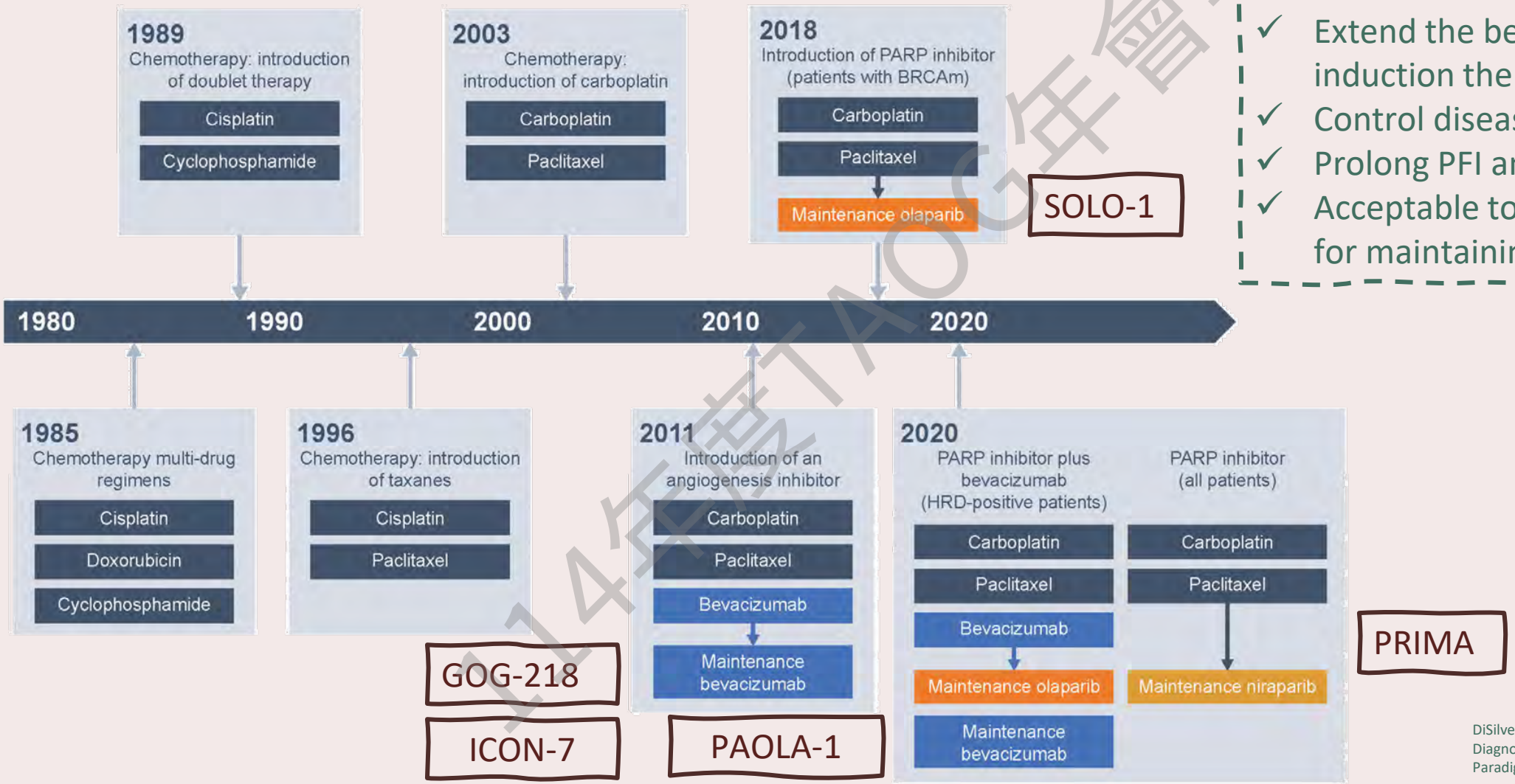
2025/3/22

The Journey of Ovarian Cancer



Once recur, it always recurs…

Maintenance Therapy



Goals of Maintenance Therapy:

- ✓ Extend the benefit of induction therapy
- ✓ Control disease for longer
- ✓ Prolong PFI and PFS
- ✓ Acceptable toxicity profile for maintaining QoL

DiSilvestro, P, et al. Maintenance Treatment of Newly Diagnosed Advanced Ovarian Cancer: Time for a Paradigm Shift? Cancers 2021, 13, 5756.

NCCN Guidelines Version 1.2025
Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer

NCCN Guidelines Index
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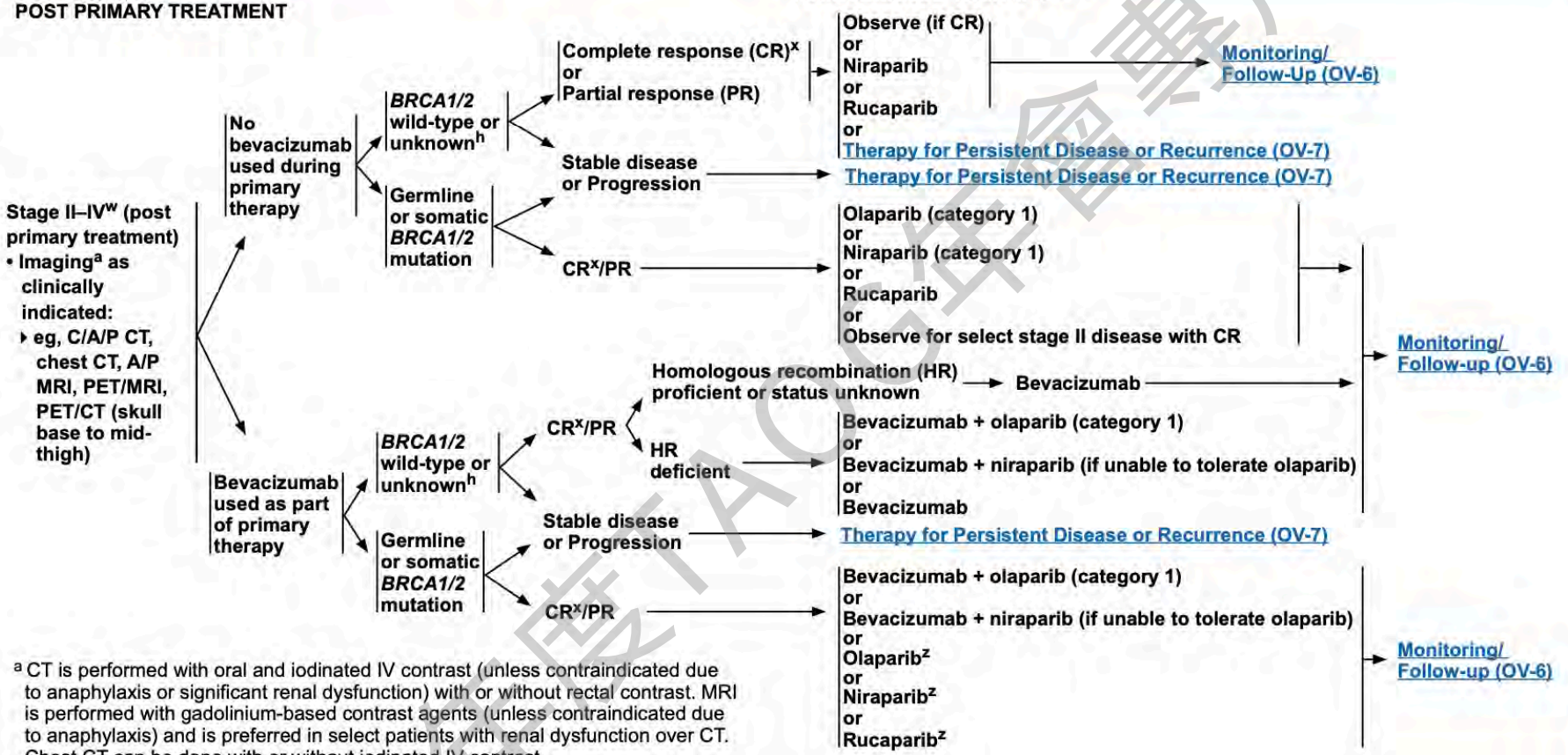
Discussion

STAGE II, III, IV[w]
POST PRIMARY TREATMENT

MAINTENANCE THERAPY[h,n,y]



[a] CT is performed with oral and iodinated IV contrast (unless contraindicated due to anaphylaxis or significant renal dysfunction) with or without rectal contrast. MRI is performed with gadolinium-based contrast agents (unless contraindicated due to anaphylaxis) and is preferred in select patients with renal dysfunction over CT. Chest CT can be done with or without iodinated IV contrast.

[h] In the absence of a *BRCA1/2* mutation, HRD status may provide information on the magnitude of benefit of PARPi therapy. For PARPi therapy in advanced stage disease, include measure of HR (OV-B).

[n] See Principles of Systemic Therapy (OV-C) and Management of Drug Reactions (OV-D).

[w] Post primary treatment recommendations for stage II–IV high-grade serous or grade 2/3 endometrioid carcinoma; consider for clear cell carcinoma or carcinosarcoma with a BRCA1/2 mutation.

[x] No definitive evidence of disease.

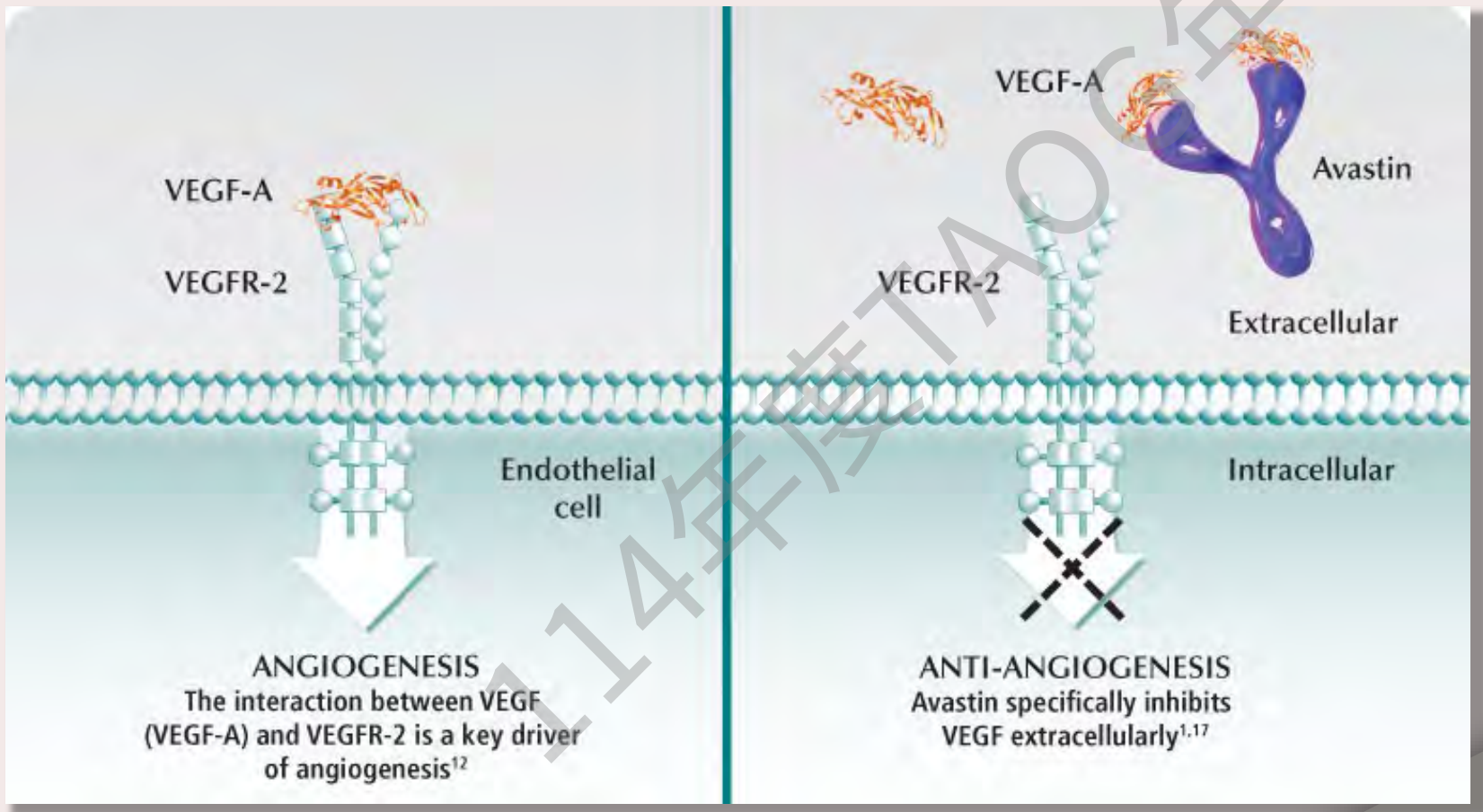
[y] Data are limited for maintenance therapy with a PARPi for patients with stage II disease.

[z] After first-line therapy with bevacizumab, data are limited on maintenance therapy with a single-agent PARPi (olaparib, niraparib, or rucaparib) for patients with a germline or somatic BRCA1/2 mutation. However, based on the magnitude of benefit of PARPi maintenance therapy for other subgroups, single-agent PARPi can be considered.

Note: All recommendations are category 2A unless otherwise indicated.

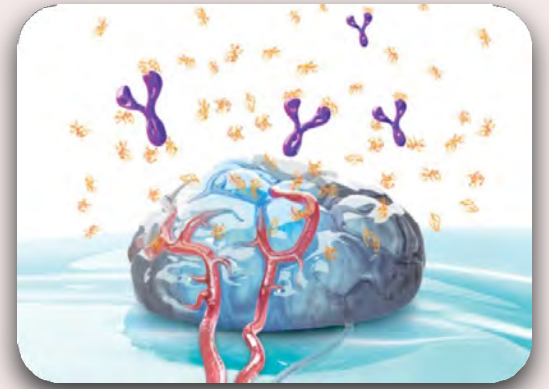
Maintenance Therapy - Bevacizumab

- Monoclonal antibody



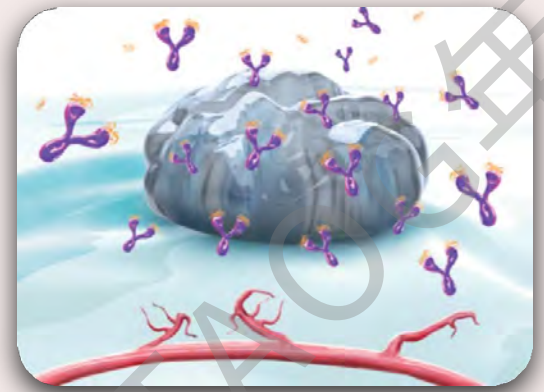
https://www.innovationhub.world/post/vegf-s-role-in-tumour-angiogenesis-and-nov
anti-angiogenic-drugs-to-treat-cancer-retinal-disease
https://www.brainkart.com/article/Bevacizumab---Classes-of-Monoclonal-Antibodies

Maintenance Therapy - Bevacizumab



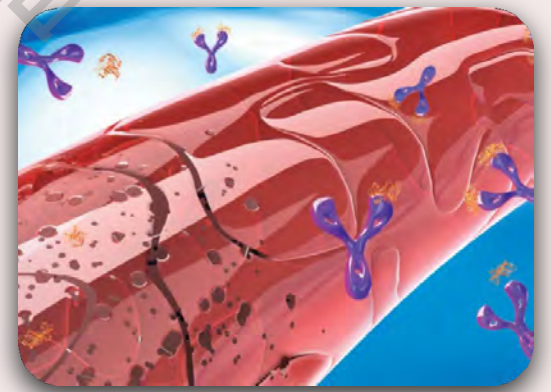
Regression

of existing tumour vasculature[1–3]



Inhibition

of new vessel growth[1–3,8]



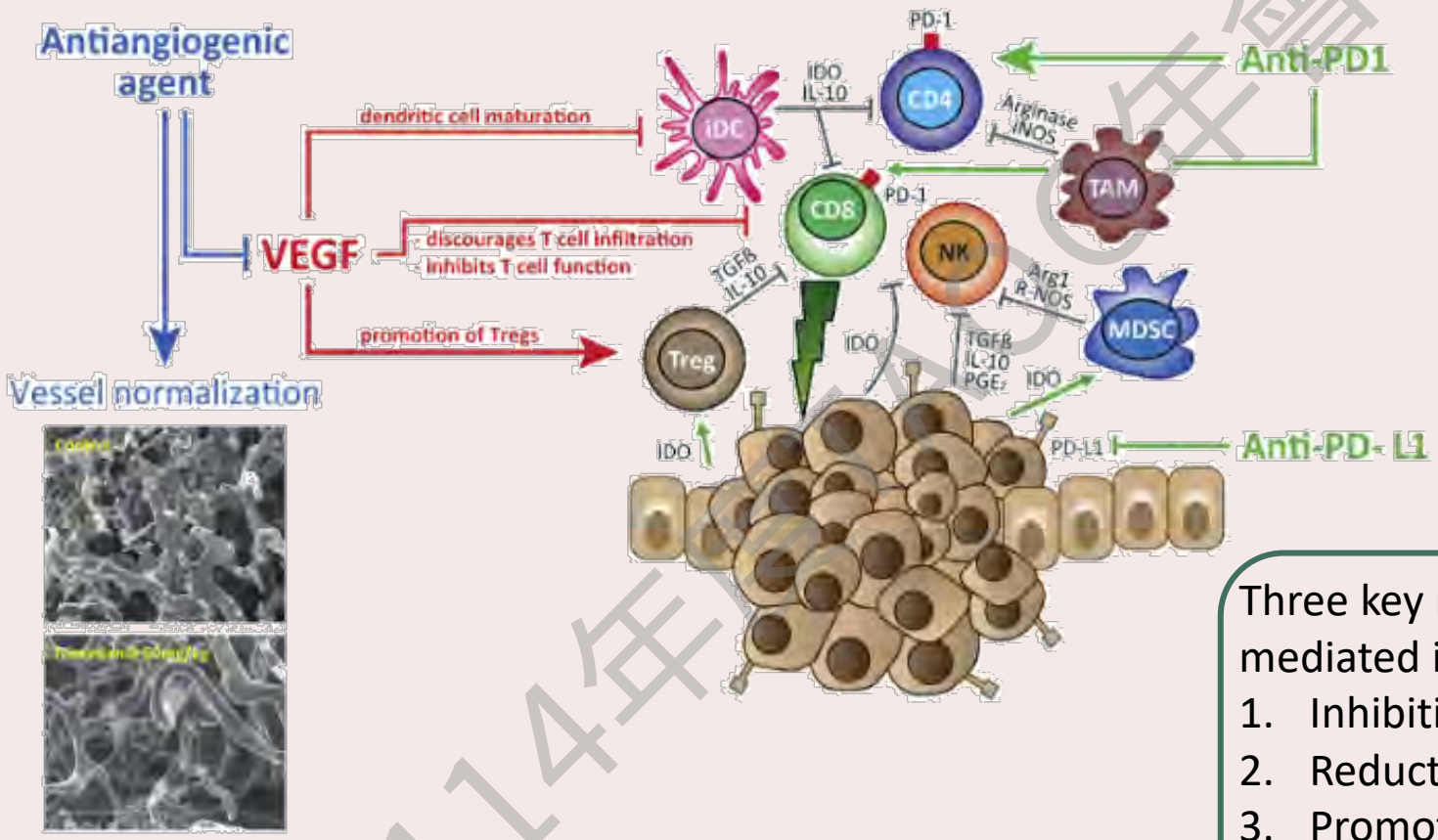
Anti-permeability

of surviving vasculature[11–13]

Consistently increased response rates[4–7]
Continuous control of tumour growth[8–10]
Reduction of ascites and effusions[2,3,11,14–

1. Baluk, et al. Curr Opin Genet Dev 2005; 2. Willett, et al. Nat Med 2004; 3. O'Connor, et al. Clin Cancer Res 2009; 4. Hurwitz, et al. NEJM 2004; 5. Sandler, et al. NEJM 2006; 6. Escudier, et al. Lancet 2007; 7. Miller, et al. NEJM 2007; 8. Mabuchi, et al. Clin Cancer Res 2008; 9. Wild, et al. Int J Cancer 2004; 10. Gerber, Ferra Cancer Res 2005; 11. Prager, et al. Mol Oncol 2010; 12. Yanagisawa, et al. Anti-Cancer Drugs 2010; 13. Dickson, et al. Clin Cancer Res 2007; 14. Hu, et al. Am J Pa 2002; 15. Ribeiro, et al. Respirology 2009; 16. Watanabe, et al. Hum Gene Ther 2009; 17. Mesiano, et al. Am J Pathol 1998; 18. Bellati, et al. Invest New Drugs 20 19. Huynh, et al. J Hepatol 2008; 20. Ninomiya, et al. J Surg Res 2009

Maintenance Therapy - Bevacizumab



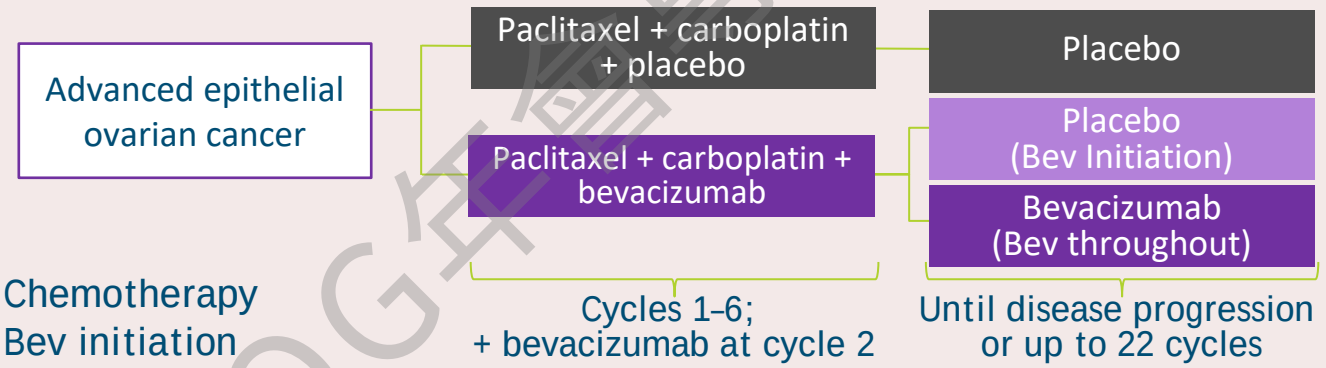
Three key mechanisms related to (VEGF)–mediated immunosuppression[1] :

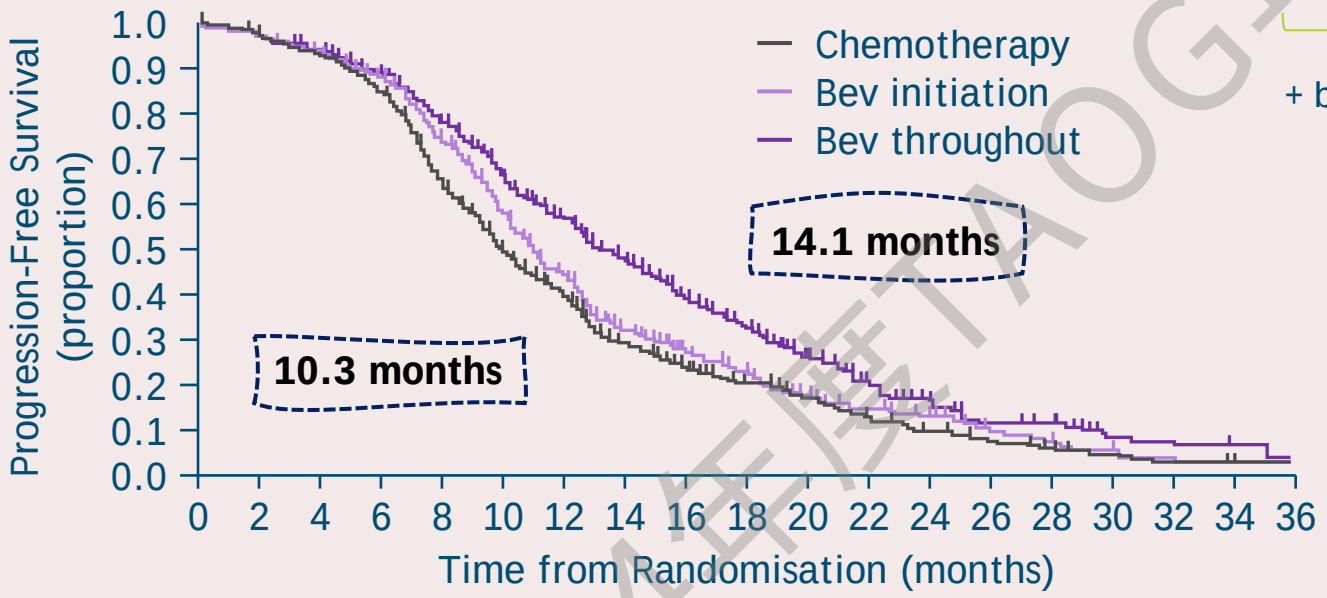
1. Inhibition of dendritic cell maturation
2. Reduction of T-cell tumor infiltration
3. Promotion of inhibitory cells in the tumor microenvironment

Daniel S. Chen, MD, PhD and Herbert Hurwitz, MD.The Cancer Journal . Volume 24, Number 4, July/August 2018

Maintenance Therapy - Bevacizumab

GOG-218





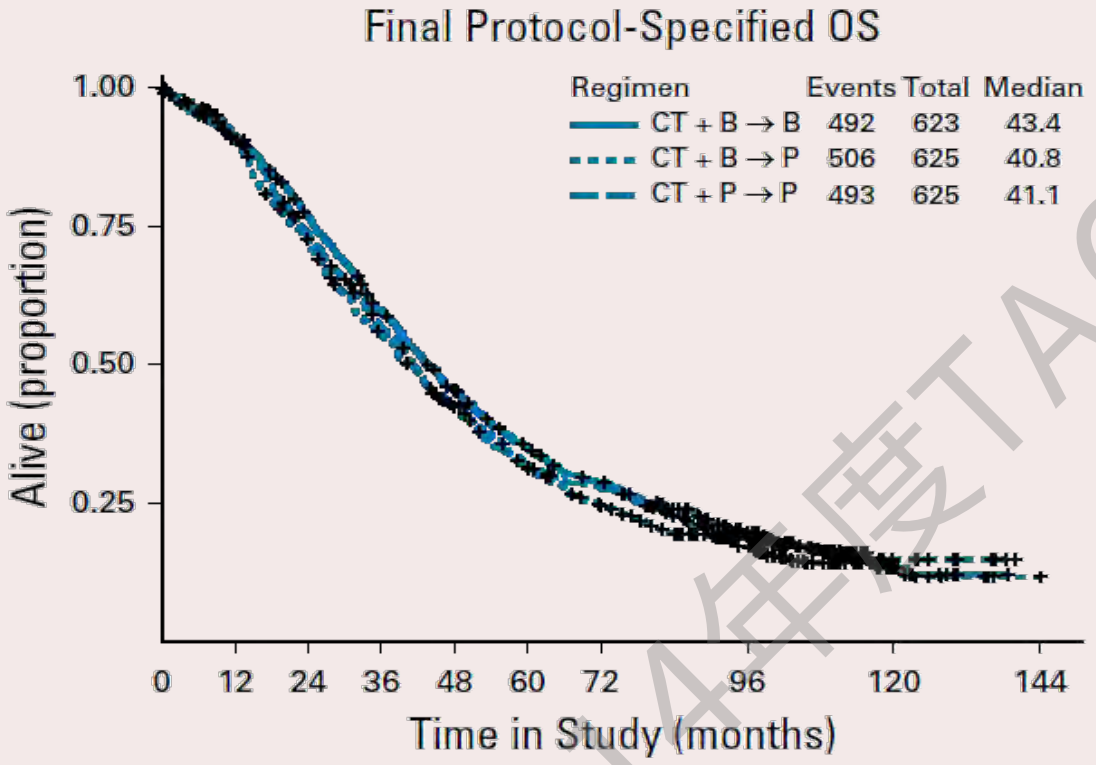
+3.8M
HR: 0.72
p<0.001

No. at risk				
Chemotherapy	625	199	33	8
Bev initiation	625	219	29	6
Bev throughout	623	254	38	8

Tewari KS, et al. Final Overall Survival of a Randomized Trial of Bevacizumab for Primary Treatment of Ovarian Cancer. J Clin Oncol. 2019 Sep 10;37(26):2317-2328

Maintenance Therapy - Bevacizumab

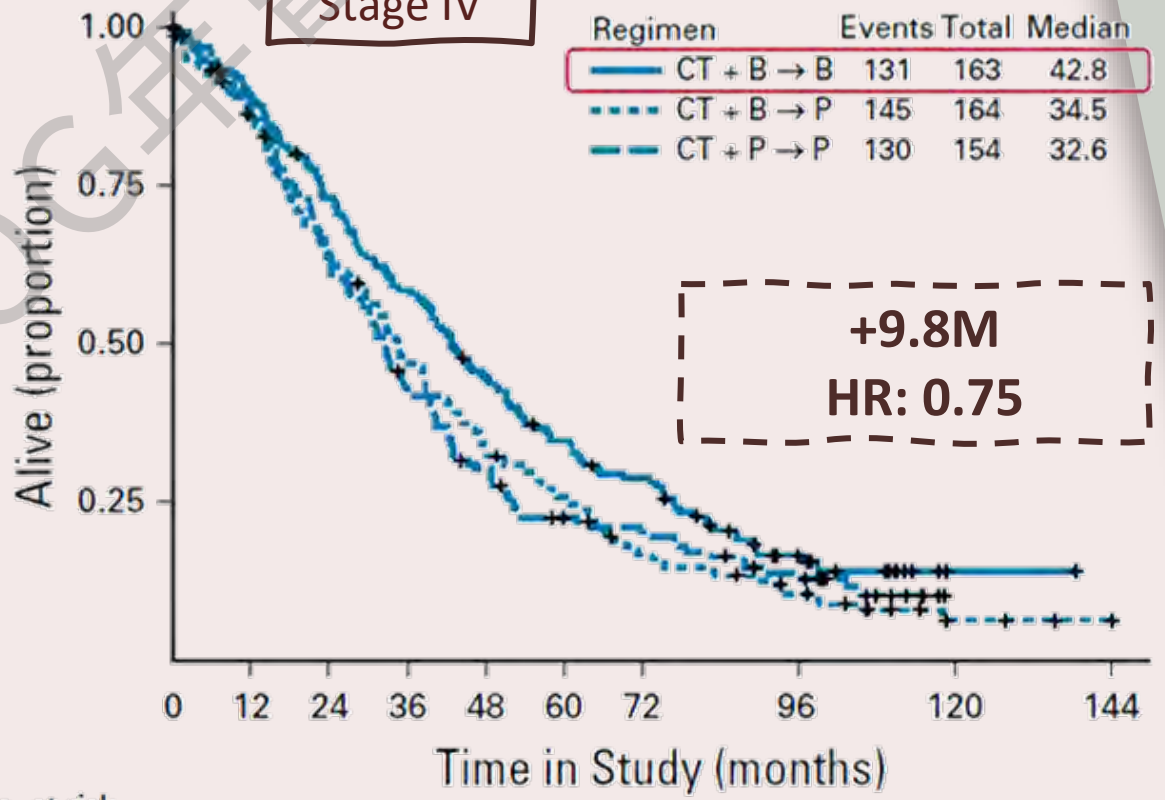
GOG-218



No. at risk

CT + B → B	623	561	464	358	267	201	161	85	11	0
CT + B → P	625	558	443	334	252	185	136	74	11	1
CT + P → P	625	558	448	340	252	183	158	90	9	0

Stage IV



No. at risk

CT + B → B	163	142	115	92	70	53	43	17	1	0
CT + B → P	164	139	104	74	51	40	25	14	3	1
CT + P → P	154	130	96	64	44	31	26	14	0	

Tewari KS, et al. Final Overall Survival of a Randomized Trial of Bevacizumab for Primary Treatment of Ovarian Cancer. J Clin Oncol. 2019 Sep 10;37(26):2317-2328

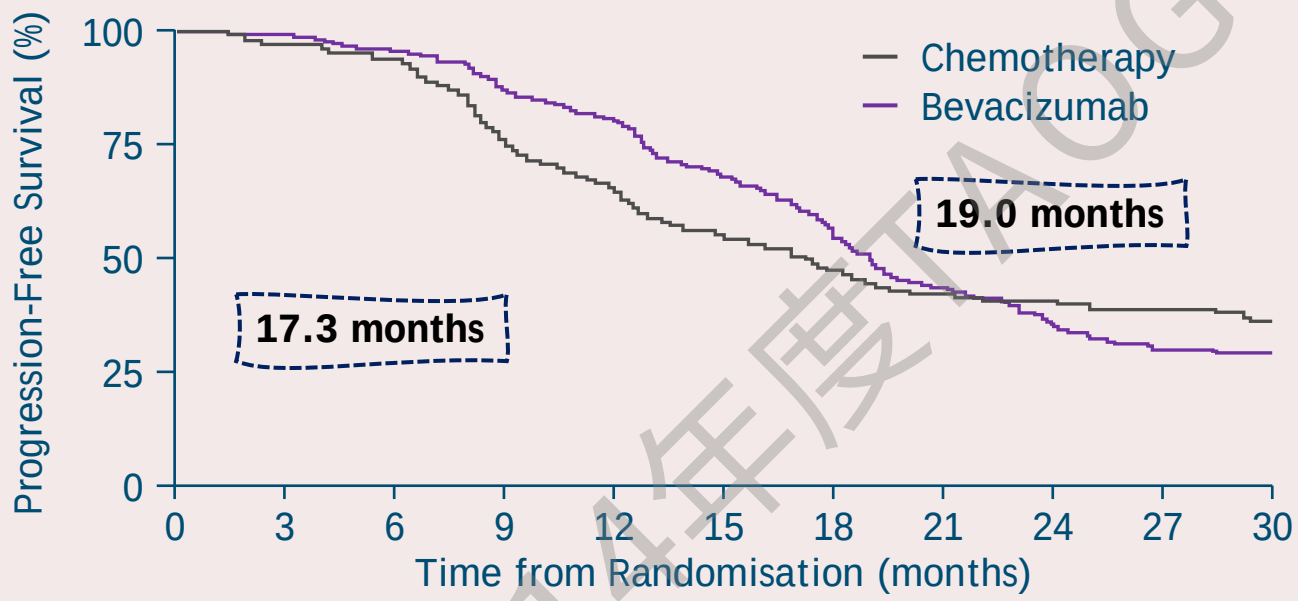
Maintenance Therapy - Bevacizumab

ICON-7

Advanced epithelial ovarian cancer

- Paclitaxel + carboplatin
- Paclitaxel + carboplatin + bevacizumab → Bevacizumab

Cycles 1–6 | Until disease progression or 12 cycles



+2.4M
HR: 0.81
p= 0.0041

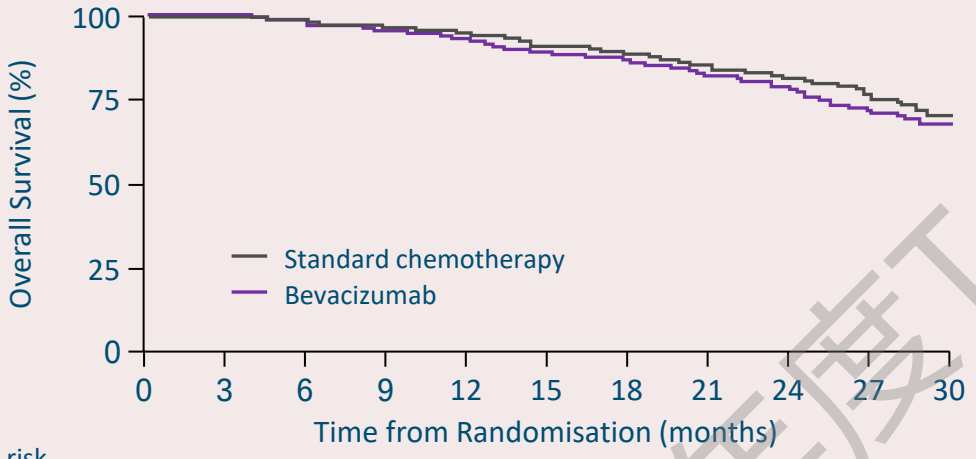
No. at risk

Chemotherapy	764	693	464	216	91	25
Bevacizumab	764	715	585	263	73	19

Oza AM, et al; ICON7 trial investigators. Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): overall survival results of a phase 3 randomised trial. Lancet Oncol. 2015 Aug;16(8):928-36.

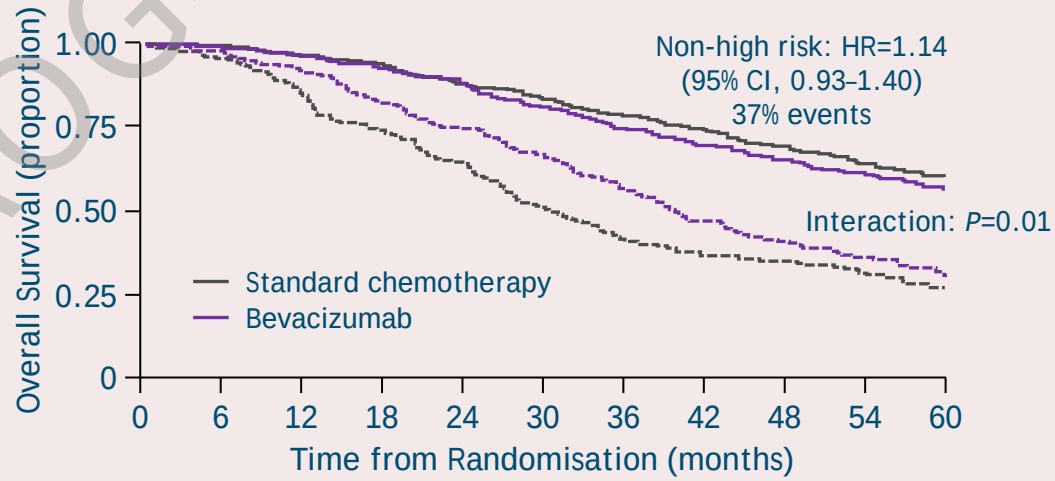
Maintenance Therapy - Bevacizumab

ICON-7



No. at risk						
Standard chemotherapy	764	724	652	368	159	33
Bevacizumab	764	737	678	404	162	40

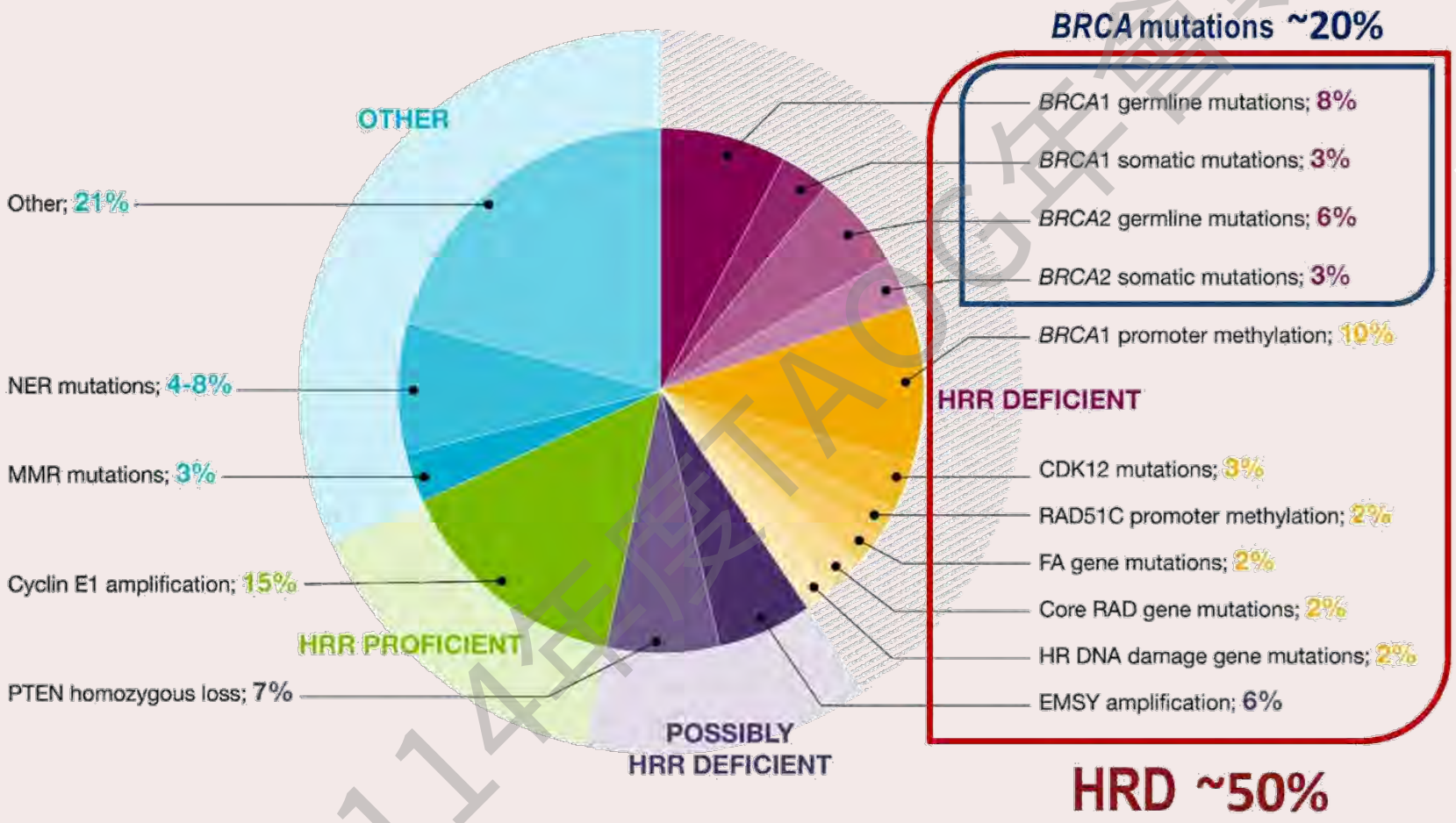
Subgroup, high risk: residual disease >1 cm/Stage IV



High risk: HR=0.78
(95% CI, 0.63–0.97)
66% events

Oza AM, et al; ICON7 trial investigators. Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): overall survival results of a phase 3 randomised trial. Lancet Oncol. 2015 Aug;16(8):928-36.

Maintenance Therapy – PARPi



***BRCA*m sensitive to PARPi**

***BRCA*wt HRD may be sensitive to PARPi**

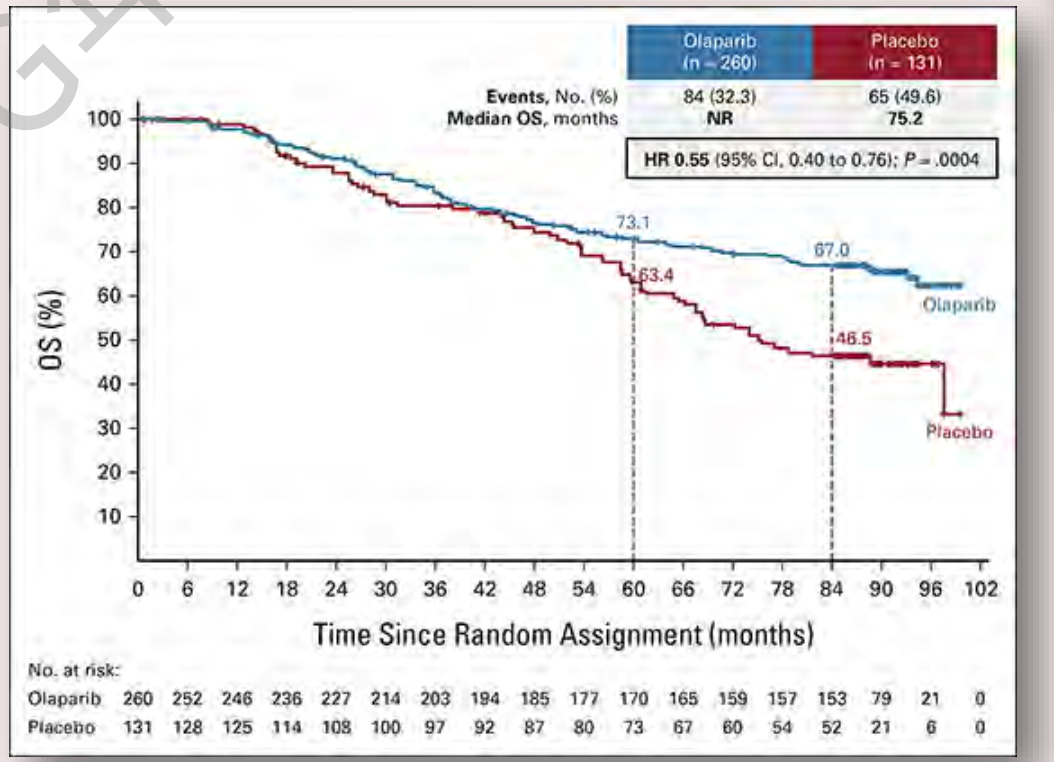
DiSilvestro P, Banerjee S, Colombo N, et al. Overall survival with maintenance olaparib at a 7-year follow-up in patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: the SOLO1/GOG 3004 trial. J Clin Oncol. 2022;JCO2201549..

Maintenance Therapy – PARPi (Olaparib)

SOLO-1

- ✓ Randomized, Phase III
- Newly diagnosed ovarian cancer
  - Stage III-IV
  - High grade serous or endometrioid type
  - Mutation in BRCA1/2
  - Complete or partial response

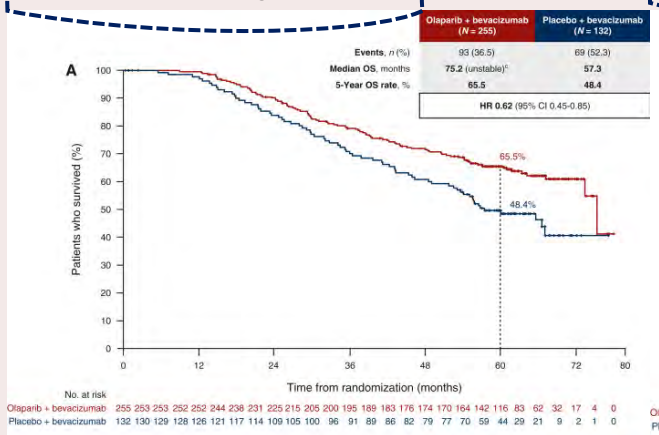
  (After Platinum-based chemotherapy)
- ✓ Olaparib 300mg, PO, BID
- ✓ Results :
- PFS (3y): 60% vs 27% (HR 0.3)
- mPFS (5y): 56m vs 13.8m (HR 0.33)
- mOS (7y): NR vs 75.2m (HR 0.55)



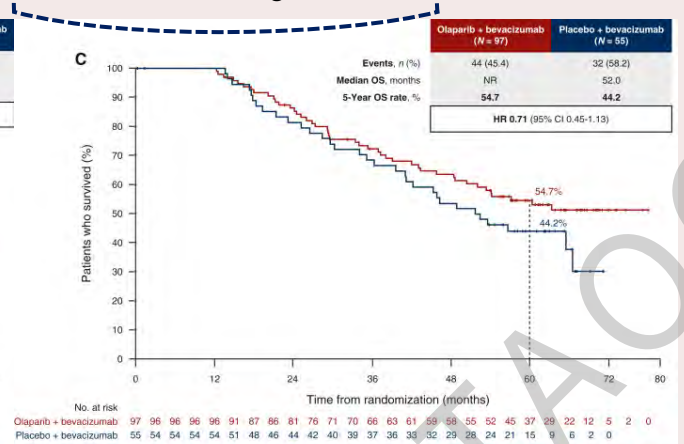
DiSilvestro P, Banerjee S, Colombo N, et al. Overall survival with maintenance olaparib at a 7-year follow-up in patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: the SOLO1/GOG 3004 trial. J Clin Oncol. 2022;JCO2201549..

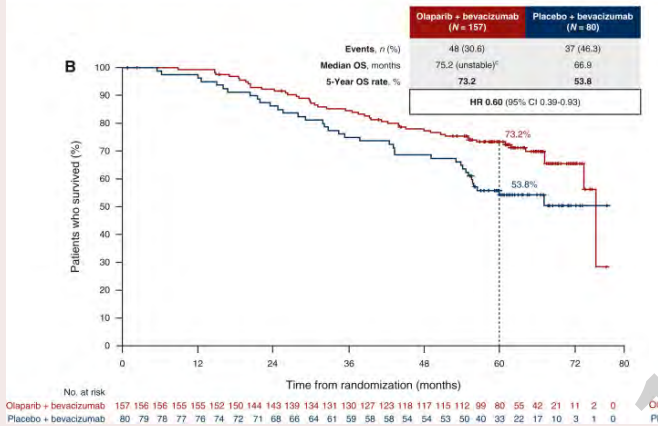
Maintenance Therapy – PARPi (Olaparib)

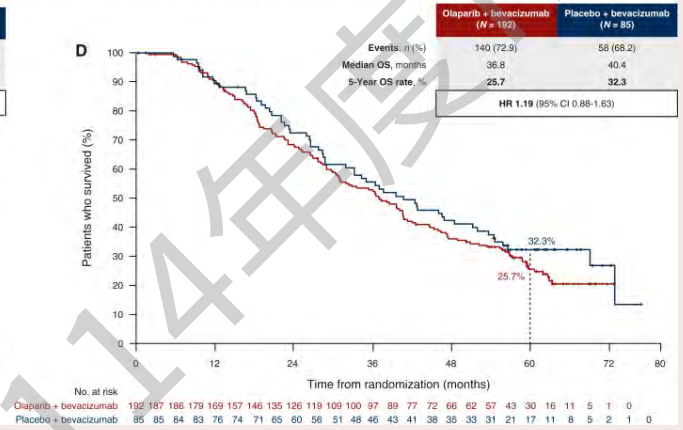
HRD, including BRCAm



HRD, excluding BRCAm







BRCAm

HRP

PAOLA-1

- ✓ **Randomized, Phase III**
- **Newly diagnosed ovarian caner**
  - **Stage III-IV**
  - **High grade serous or endometrioid type**
  - **CR/PR after C/T + bevacizumab**
- ✓ **Olaparib 300mg, PO, BID**
  Bevacizumab 15mg/kg, IV, Q3W
- ✓ **Results (PFS):**
  - **Overall: 22.1 m vs 16.6 m (HR 0.59)**
  - **BRCA ½ mut.: 37.2 m vs 21.7 m (HR 0.31)**
  - **BRCA ½ wt/ND: 18.9 m vs 16 m (HR 0.71)**
  - **BRCA ½ wt, HRD: 28.1m vs 16.6 m (HR 0.42)**
  - **HRD: 37.2 m vs 17.7 m (HR 0.33)**
  - **HRP: 16.6 m vs 16.2 m (HR 1)**

Ray-Coquard I, et al/ PAOLA-1/ENGOT-ov25 investigators. Olaparib plus bevacizumab first-line maintenance in ovarian cancer: final overall survival results from the PAOLA-1/ENGOT-ov25 trial. Ann Oncol. 2023 Aug;34(8):681-692.

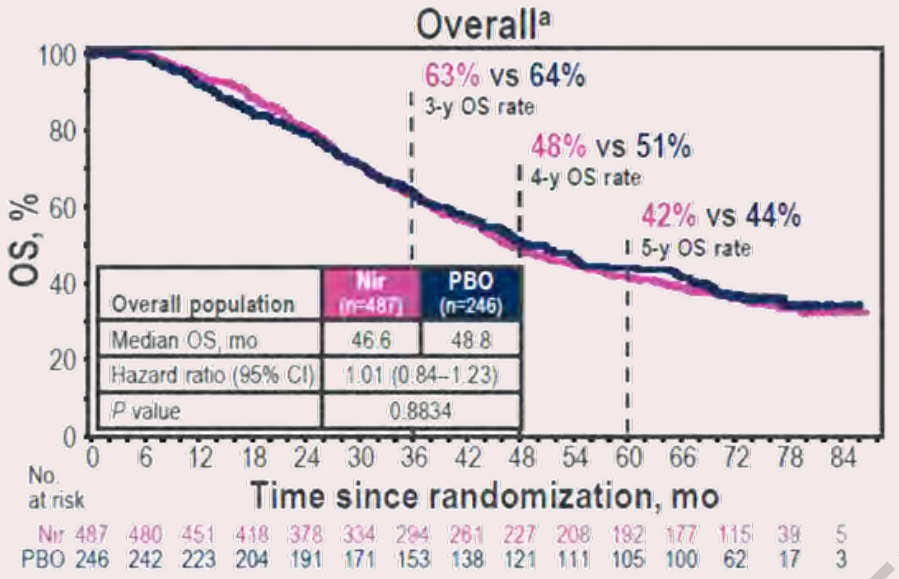
Maintenance Therapy – PARPi (Niraparib)

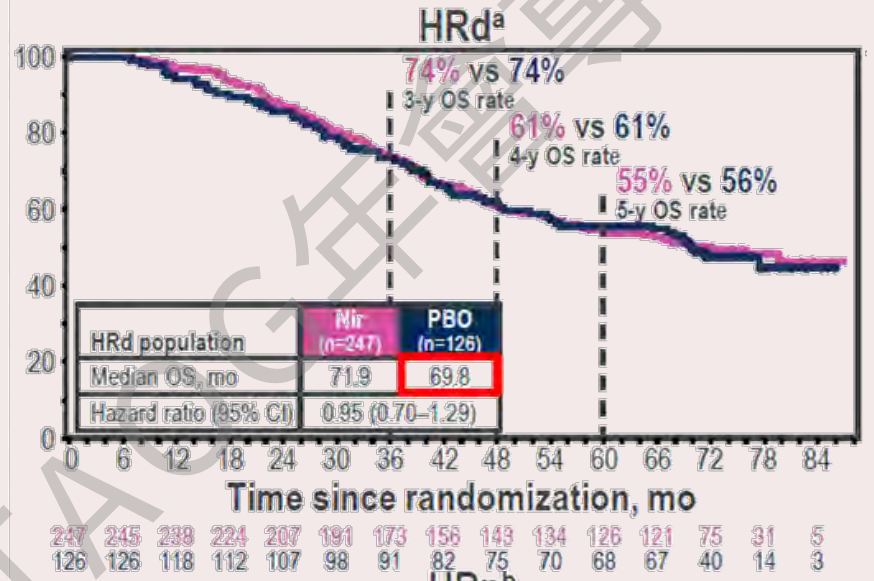
PRIMA

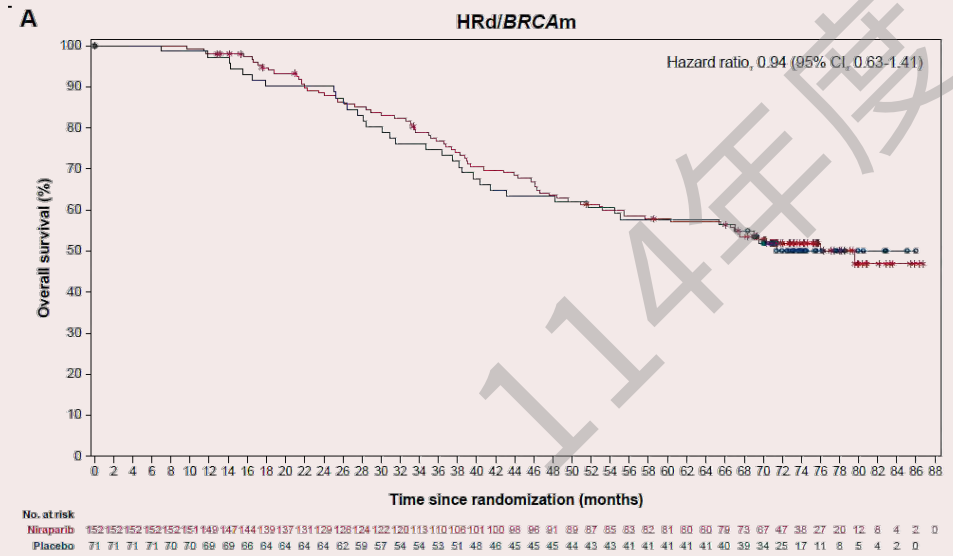
- ✓ Randomized, Phase III
- Newly diagnosed ovarian cancer
  - Stage III-IV
  - High grade serous or endometrioid type
  - Complete or partial response (After Platinum-based chemotherapy)
- ✓ Niraparib 300mg, PO, QD
- ✓ Results (PFS) :
- Overall: 13.8 months vs 8.2 months (HR 0.62)
- HRD: 21.9 months vs 10.4 months (HR 0.43)
- BRCA ½ mut.: 22.1 months vs 10.9 months (HR 0.4)
- BRCA ½ wt, HRD: 19.2months vs 8.2 months (HR 0.5)
- HRP: 8.1 months vs 5.4 months (HR 0.68)

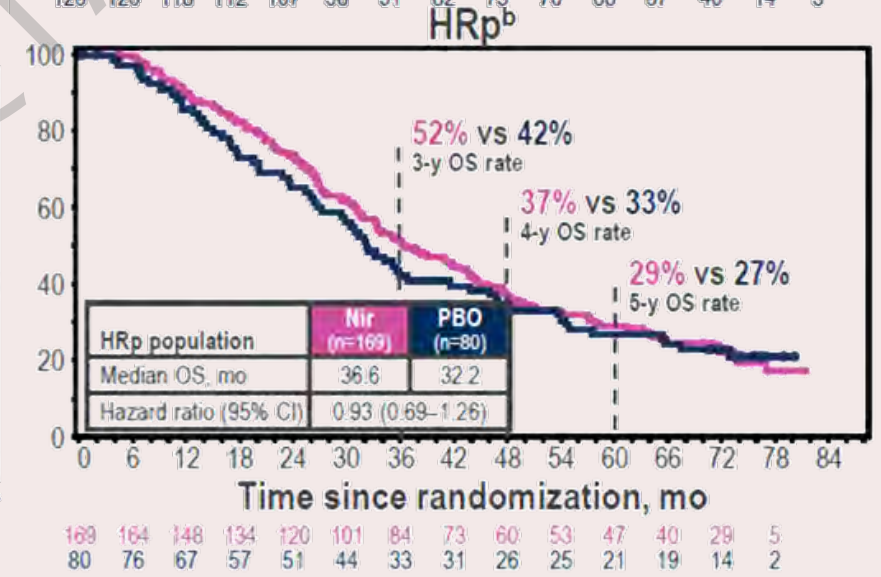
DiSilvestro P, Banerjee S, Colombo N, et al. Overall survival with maintenance olaparib at a 7-year follow-up in patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: the SOLO1/GOG 3004 trial. J Clin Oncol. 2022;JCO2201549..

Maintenance Therapy – PARPi (Niraparib)









DiSilvestro P, Banerjee S, Colombo N, et al. Overall survival with maintenance olaparib at a 7-year follow-up in patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: the SOLO1/GOG 3004 trial. J Clin Oncol. 2022;JCO2201549..

Maintenance Therapy – PARPi (Niraparib)

OVARIO

Niraparib +/- Bevacizumab

Objective

- Assess the safety and efficacy of combination niraparib (PARP inhibitor) + bevacizumab (anti-angiogenic agent) as a first-line maintenance therapy for patients with newly diagnosed advanced ovarian cancer

Design: Phase II, Single-Arm, Open-Label Study

Patients with newly diagnosed high-grade serous or endometrioid stage IIIB or IV epithelial ovarian, fallopian tube, or peritoneal cancer who achieved a CR, PR, or NED result after front-line platinum-based chemotherapy + bevacizumab (N=105)

All patients underwent tissue testing for HRD status at enrollment

Niraparib (200 or 300 mg QD) + bevacizumab (15 mg/kg Q3W)

Niraparib starting dose

200 mg: <77 kg and/or platelet count <150,000/μL

300 mg: All others

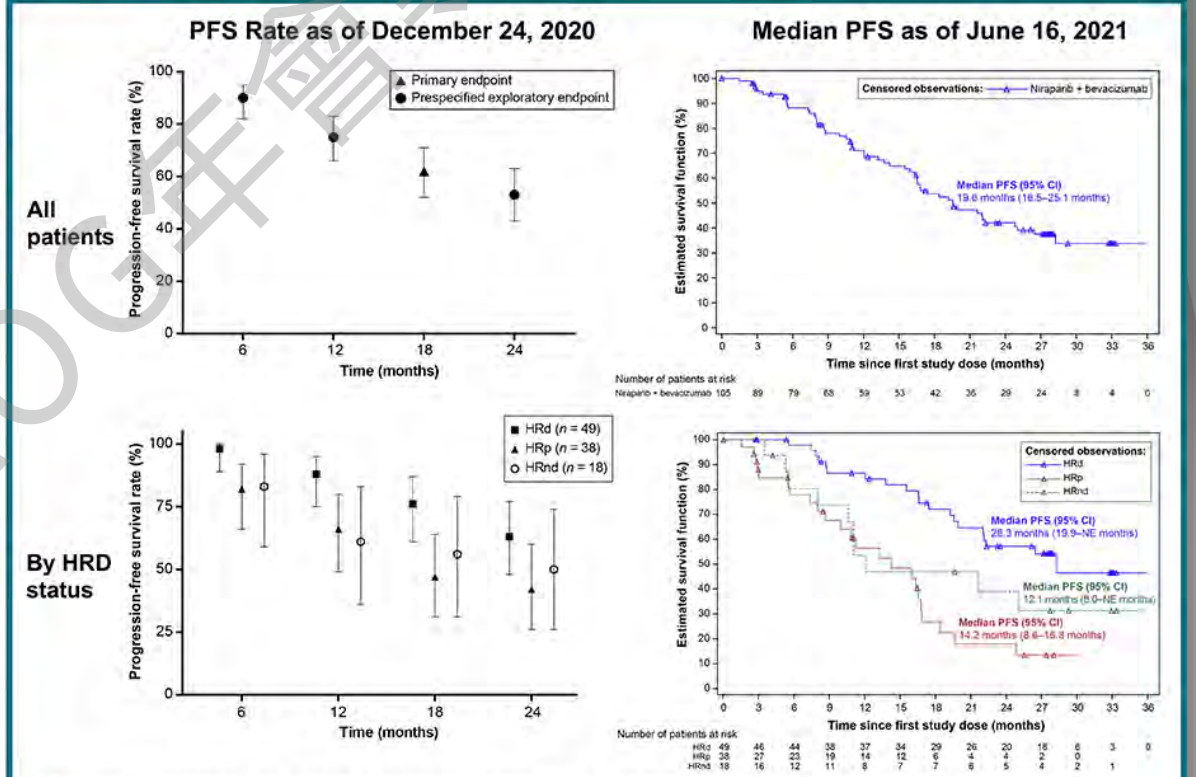
Bevacizumab

Maximum of 15 months, including first-line treatment

Endpoint		Data cutoff
Efficacy	PFS rate at 18 months[a]	December 24, 2020
	Median PFS	June 16, 2021
Safety	Treatment-related AEs	December 24, 2020

[a]Primary endpoint.

Results



The most common any-grade treatment-related AEs (related to niraparib and/or bevacizumab) were thrombocytopenia (74/105, 70.5%), fatigue (60/105, 57.1%), and anemia (55/105, 52.4%; June 16, 2021, clinical cutoff date)

Conclusion

- Niraparib + bevacizumab first-line maintenance therapy displayed promising PFS results
- Safety was consistent with the known safety profiles of niraparib and bevacizumab as monotherapies

Abbreviations: AE, adverse event; CR, complete response; HRD, homologous recombination deficiency; HRd, homologous recombination deficient; HRnd, homologous recombination not determined; HRp, homologous recombination proficient; NED, no evidence of disease; PARP, poly(ADP-ribose) polymerase; PFS, progression-free survival; PR, partial response; Q3W, every 3 weeks; QD, every day.

Maintenance Therapy – PARPi (Niraparib)

NIRVANA-1
(Phase II)

Niraparib +/- Bevacizumab

NIRVANA-1/GINECO-ov129b/ENGOT-ov63: A multicentre randomized study comparing carboplatin-paclitaxel (CP) followed by niraparib (nira) to CP–bevacizumab (bev) followed by nira-bev in patients with FIGO Stage III ovarian high-grade epithelial cancer and no residual disease after upfront surgery

Authors: *Gilles FREYER [1], Antonio GONZALEZ MARTIN [2], Francesco RASPAGLIESI [3], Julien PERON [1], Els VAN NIEUWENHUYSEN [4], Kosei HASEGAWA [5], Myong Cheol LIM [6], Isabelle RAY-COQUARD [7]*

Affiliation : [1] Hospices Civils de Lyon, Lyon, France and Groupe d'Investigateurs Nationaux pour l'Étude des Cancers de l'Ovaire et du sein (GINECO), France; [2] Clinica Universidad de Navarra, Madrid, Spain and Grupa Español de Investigación en Cáncer de Ovario (GEICO), Spain; [3] Istituto Nazionale Tumori, Milano, Italy and Mario Negri Gynecologic Oncology group (MaNGO), Italy; [4] Leuven Cancer Institute, University Hospital Leuven, Belgium and Belgium and Luxembourg Gynaecological Oncology Group (BGOG), Belgium; [5] Saitama Medical University International Medical Center, Saitama, Japan and Gynecologic Oncology Trial and Investigation Consortium (GOTIC), Japan; [6] Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Republic of Korea and Korean Gynecologic Oncology Group (KGOG), Korea; [7] Centre Léon Bérard, Lyon, France and GINECO, France

Poster #615TiP

INTRODUCTION / BACKGROUND

The standard treatment for advanced high-grade ovarian carcinoma (AdHGOC) is upfront complete surgery followed by adjuvant platinum-taxane chemotherapy. The most common maintenance strategies include bevacizumab and PARP inhibitors. Following the results of the PRIMA (Gonzales Martin, et al. NEJM 2019) and PAOLA-1 (Ray-Coquard, et a.l NEJM 2019) studies, the most effective maintenance strategy for FIGO stage III patients still remains to be defined, between PARPi alone and PARPi + Bev. It is the purpose of the NIRVANA-1 trial.

METHODOLOGY

- NIRVANA-1 is an international randomized, open-label, phase II trial.
- 390 FIGO stage III patients with completely resected AdHGOC, receive a first CP cycle and are randomized (1:1) to receive either 5 additional CP cycles followed by maintenance with nira or 5 cycles of CP + bev followed by maintenance with nira + bev. The total treatment duration will be 24 months for nira in both arms and 15 months for bev.
- Stratification factors include tumor *BRCA* status, FIGO stage (IIIA versus IIIB/IIIC) and use of hyperthermic intraperitoneal chemotherapy during surgery, notably within the OVHIPEC2 trial.

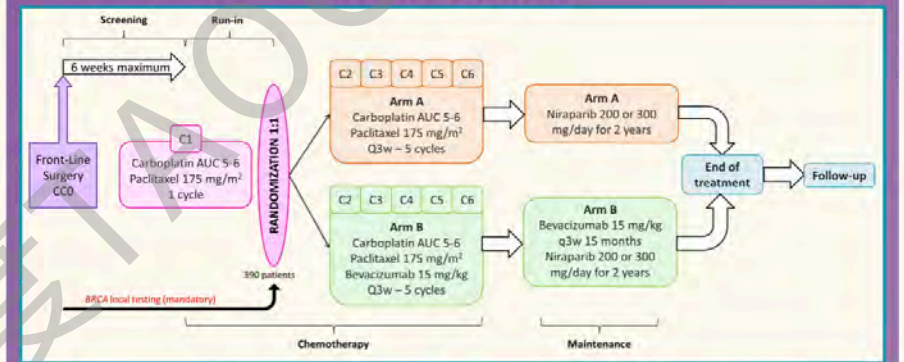
MAIN ENDPOINTS

- The primary endpoint will be the progression-free survival rate at 24 months.
- Secondary endpoints include safety, median PFS, PFS2, Time to First Subsequent Therapy (TFST), Time to Second Subsequent Therapy (TSST), OS, KELIM (K CA-125 ELIMination rate constant).

STATISTICS

- The study is designed to show a superiority of the Niraparib + Bev arm, corresponding to a 24-months PFS rate of 75% in the nira + bev arm and a 24-months PFS rate of 65% in the nira arm, translating in a HR of 0.67.
- The sample size is calculated to provide an 80% power to show a statistically significant PFS difference, accepting a 1-sided alpha risk of 10%, considering a minimal follow-up of 24 months, and dropout rate of 5%.

STUDY DESIGN



POPULATION

- Stage IIIA/B/C
- High-grade non-mucinous and non-clear cell epithelial ovarian, fallopian tube or primary peritoneal carcinoma
- Complete cytoreduction
- *BRCA* status mandatory
- PS 0/1

STRATIFICATION

- Tumor *BRCA* status (local assessment)
- FIGO stage at diagnosis (IIIA versus IIIB/IIIC)
- Previous hyperthermic intraperitoneal chemotherapy (yes/no).

PARTICIPATING GROUPS

GINECO (Groupe des Investigateurs Nationaux pour l'Etude des Cancers de l'Ovaire et du sein)
ENGOT (European Network for Gynaecological Oncological Trial groups)

ACCRUAL AND STUDY CALENDAR

- The NIRVANA-1/GINECO-OV129b/ENGOT-ov63 trial is sponsored by the GINECO and currently recruiting in France, Spain, Italy, Belgium, Japan and Korea.

- The first patient was randomized in March 2022.
- NCT 05183984
- As of Aug. 24th 2022, 16 patients have been registered. 6 patients have been randomized.
- The duration of the inclusion period is estimated around 24 months.

SUMMARY

NIRVANA-1 study will assess the potential benefit of combining bevacizumab and niraparib in patients with curable disease. In those patients, PFS and OS still can be considered as unmet needs to date.

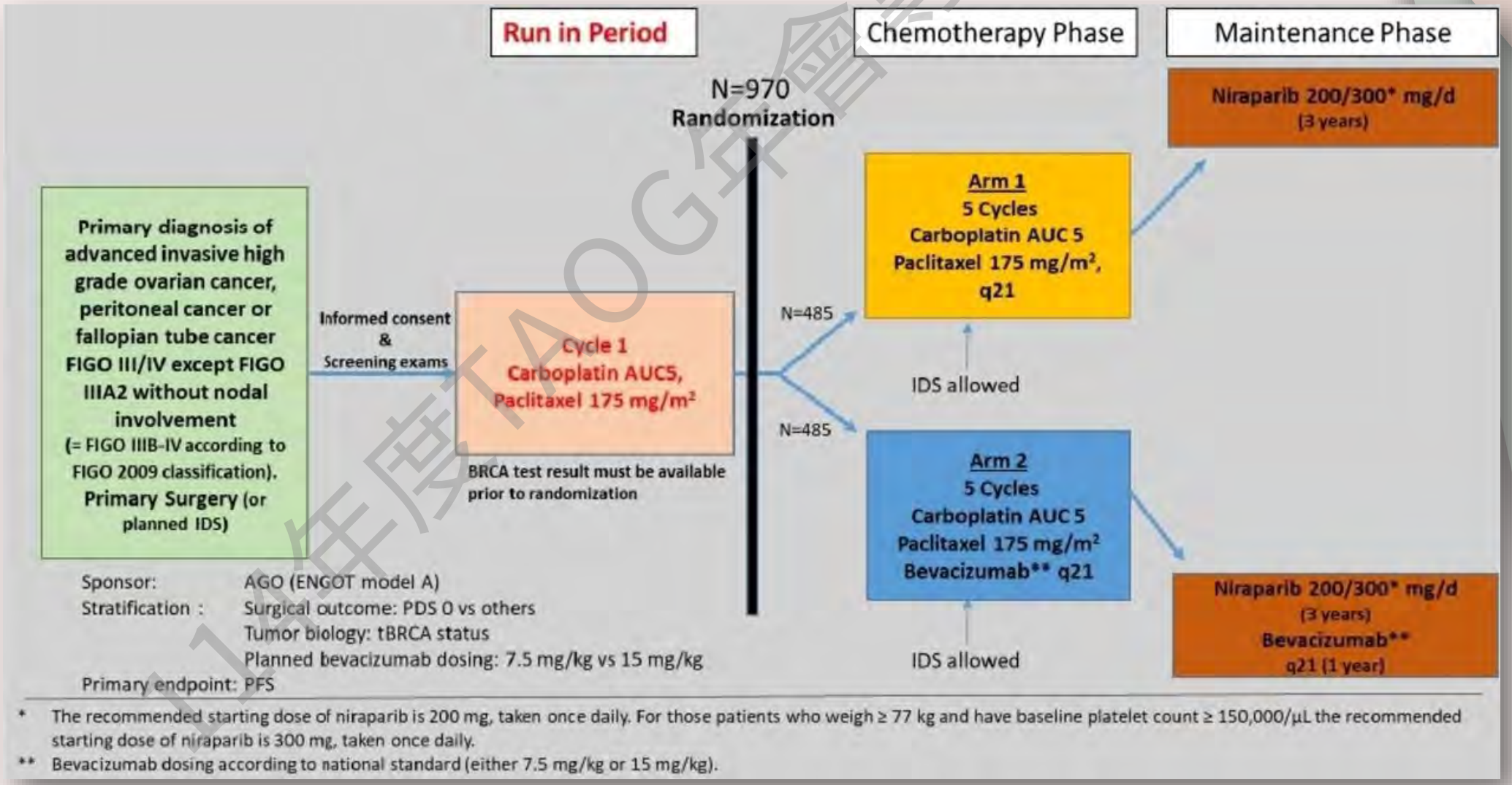
ACKNOWLEDGMENTS

- Thanks to all the patients and their families, the investigators, study nurses, pharmacists, and all study team.
- GSK provided the funding for this study.
GSK was provided the opportunity to review a preliminary version of this poster for factual accuracy, but the authors are solely responsible for final content and interpretation

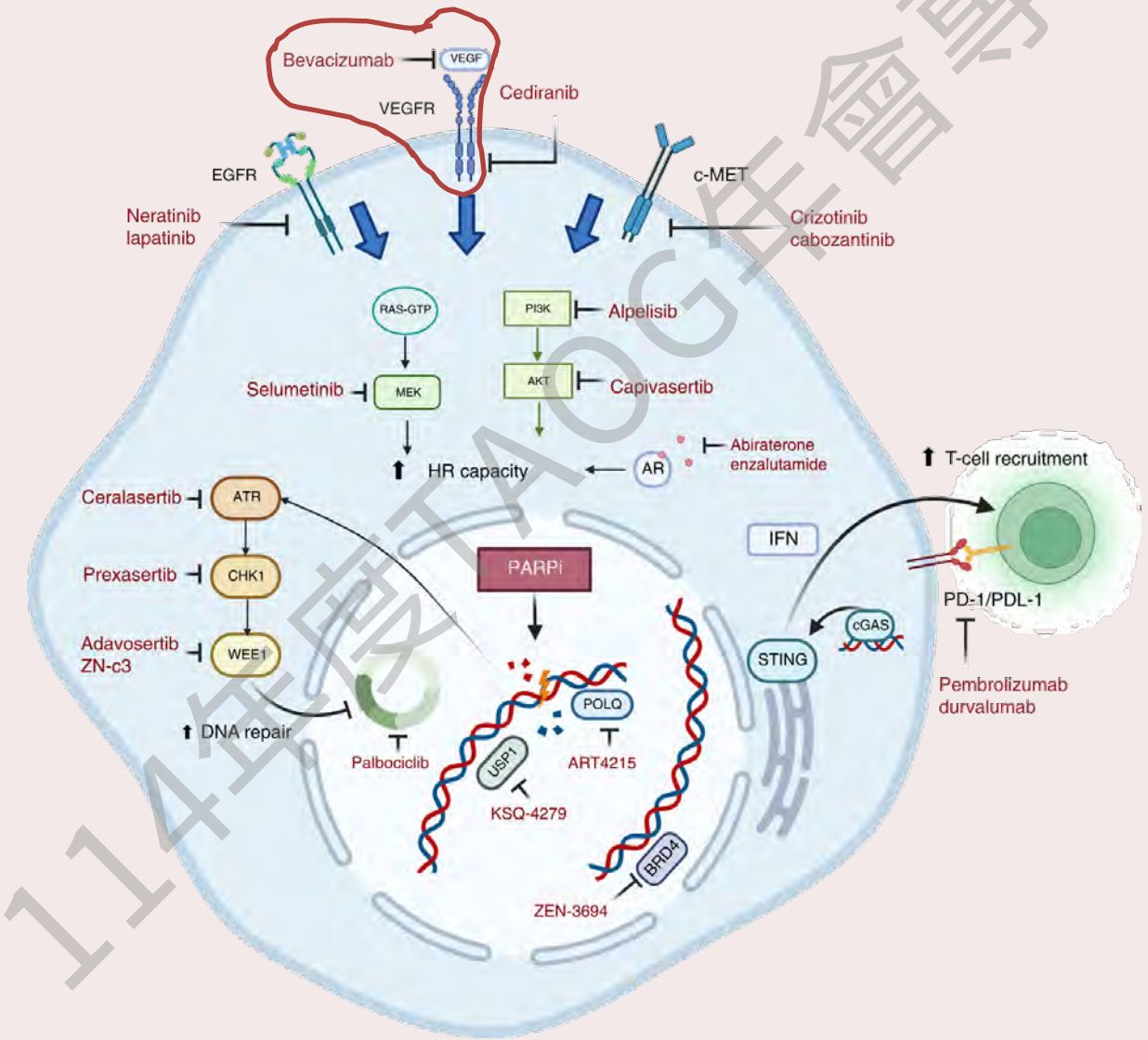
Maintenance Therapy – PARPi (Niraparib)

AGO-OVAR 28 /ENGOT-ov57
(Phase III)

Niraparib +/- Bevacizumab

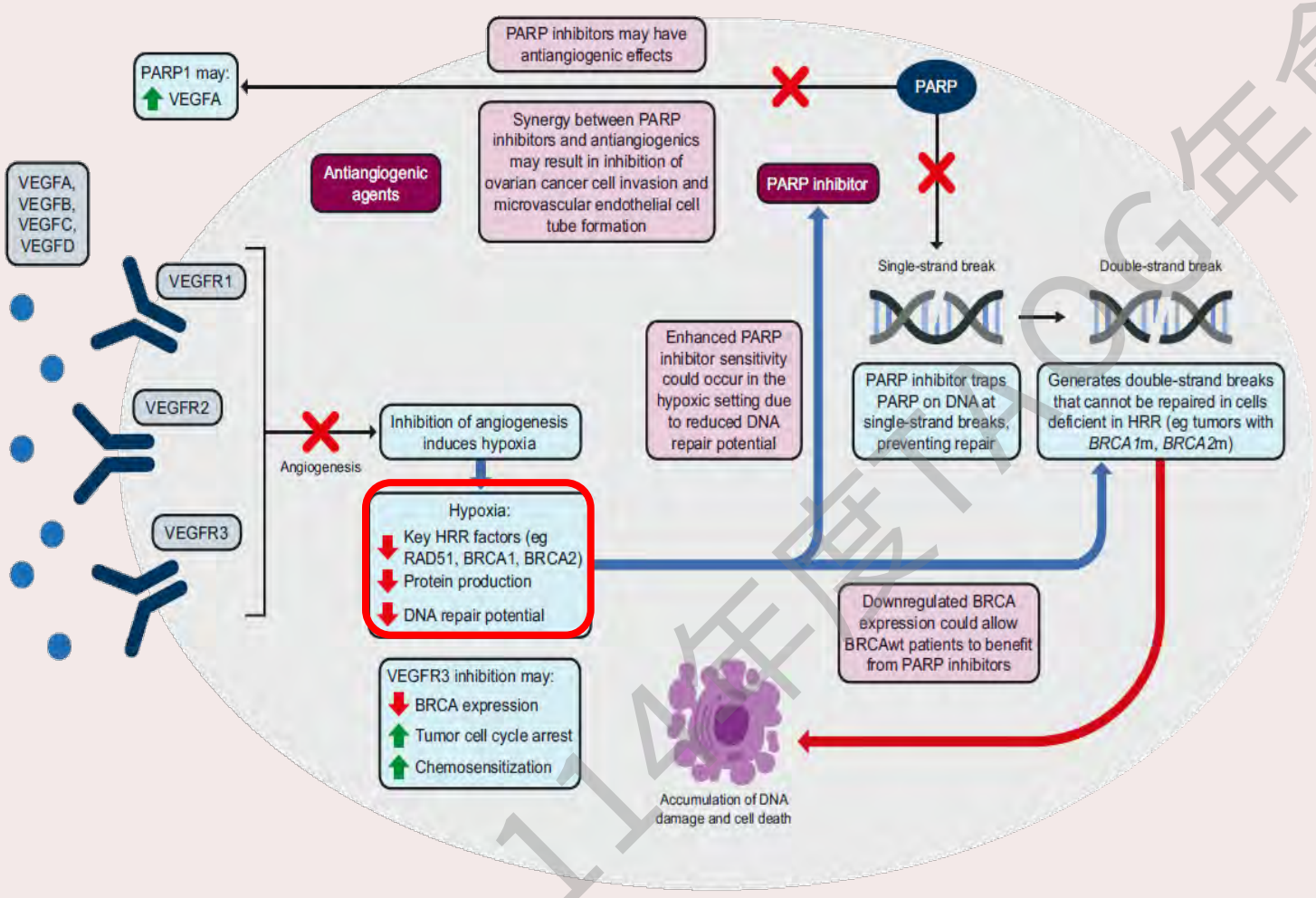


Maintenance Therapy – PARPi Combination



Bhamidipati, D., Haro-Silerio, J.I., Yap, T.A. et al. PARP inhibitors: enhancing efficacy through rational combinations. Br J Cancer 129, 904–916 (2023). https://doi.org/10.1038/s41416-023-02326-7

Maintenance Therapy – PARPi + Bevacizumab



- **Bevacizumab:**

  By inhibiting angiogenesis, antiangiogenic agents induce hypoxia in the tumor microenvironment

  → downregulating BRCA1/2 and RAD51, key factors involved in HRR gene expression and protein production.

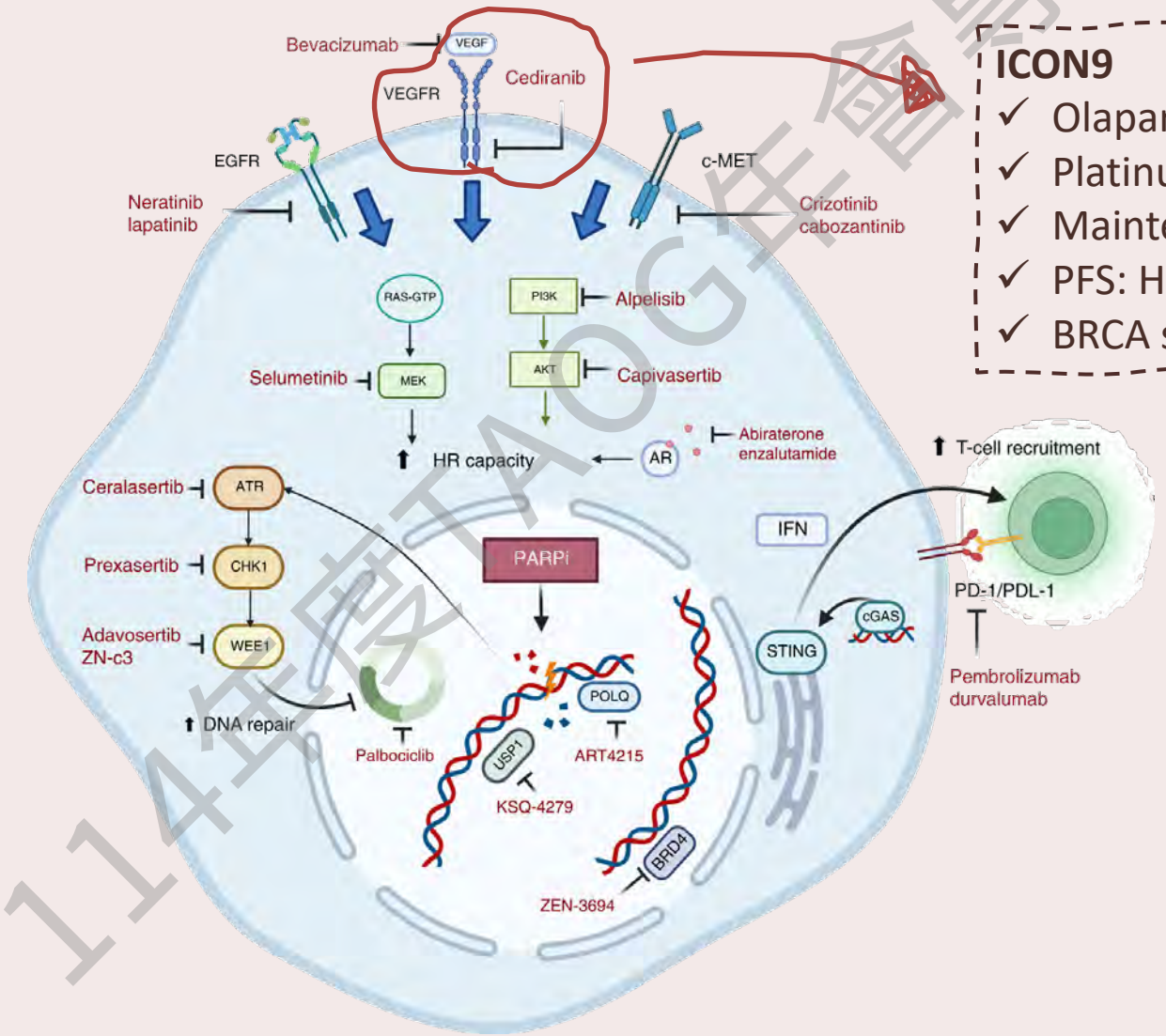
  → DNA double-strand breaks cannot be repaired

- **PARP inhibitors**

  → inhibit single-strand break repair

Angeles Alvarez Secord, et al. Gynecol Oncol. 2021 Aug;162(2):482-495

Maintenance Therapy – PARPi Combination

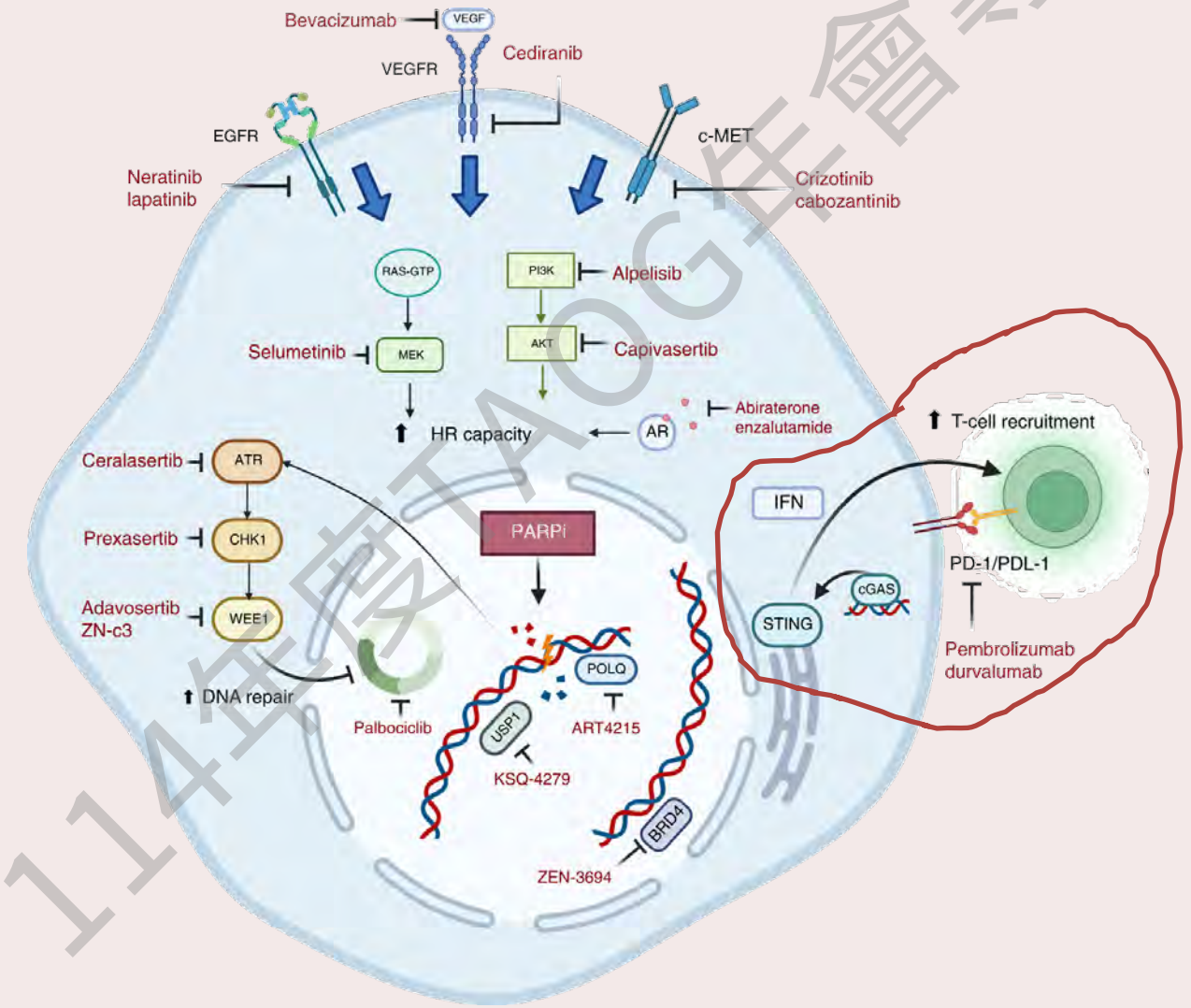


ICON9

- ✓ Olaparib +/- Cediranib
- ✓ Platinum-sensitive HGSOC
- ✓ Maintenance
- ✓ PFS: HR 0.84; OS: HR 0.92
- ✓ BRCA status: no differnece

Bhamidipati, D., Haro-Silerio, J.I., Yap, T.A. et al. PARP inhibitors: enhancing efficacy through rational combinations. Br J Cancer 129, 904–916 (2023). https://doi.org/10.1038/s41416-023-02326-7

Maintenance Therapy – PARPi Combination

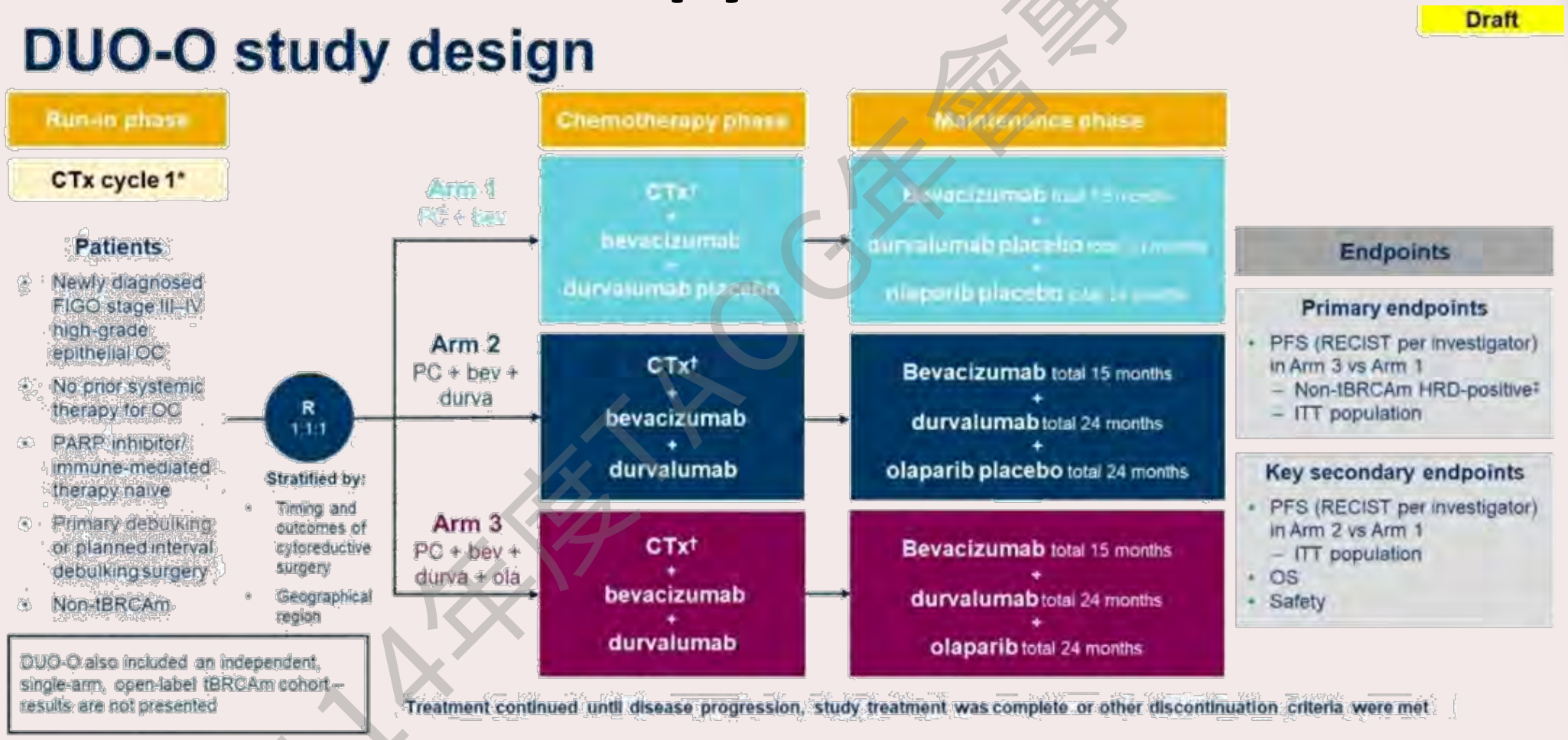


DUO-O

ATHENA-Combo

Bhamidipati, D., Haro-Silerio, J.I., Yap, T.A. et al. PARP inhibitors: enhancing efficacy through rational combinations. Br J Cancer 129, 904–916 (2023). https://doi.org/10.1038/s41416-023-02326-7

Maintenance Therapy – PARPi + ICI



Dosing and schedule: bevacizumab (15 mg/kg IV q3w); durvalumab (1120 mg IV q3w); olaparib (300 mg po bid); chemotherapy: paclitaxel 175 mg/m² IV q3w and carboplatin at AUC5 or AUC6 IV q3w. PFS interim analysis: DCO December 5, 2022.
*With or without bevacizumab according to local practice. †Cycles 2–6. ‡Genomic instability score ≥ 42 assessed prospectively by Myriad MyChoice CDx assay.
AUC, area under the curve; bev, bevacizumab; bid, twice daily; CTx, chemotherapy; DCO, data cutoff; durva, durvalumab; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; ITT, intent-to-treat; IV, intravenous; ola, olaparib; OS, overall survival; PC, paclitaxel/carboplatin; po, by mouth; q3w, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria for Solid Tumors.

Harter P, Trillisch F, Okamoto A, et al: 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. 2023 ASCO Annual Meeting. Abstract LBA5506. Presented June 3, 2023.

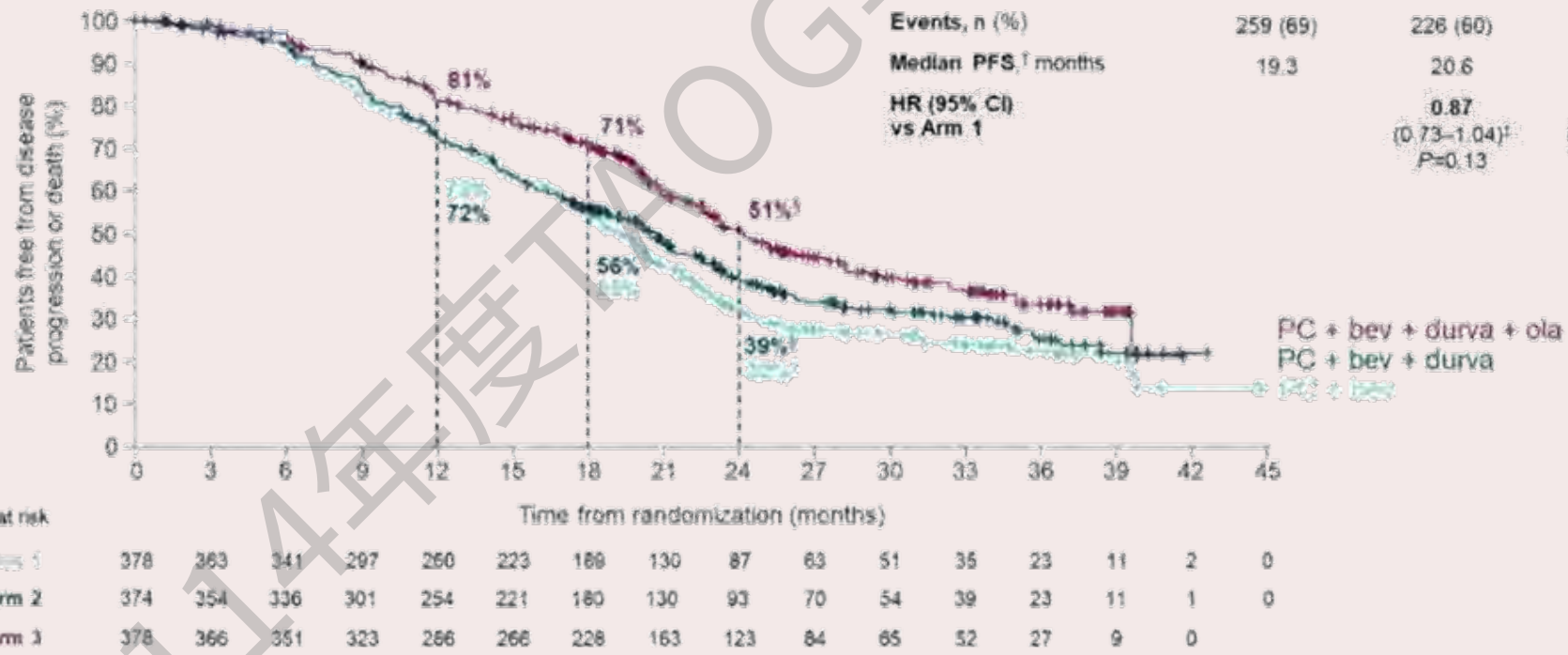
Maintenance Therapy – PARPi + ICI

PFS: ITT population

DUO-O

Draft

	Arm 1 PC + bev N=178	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	

*In censored patients. †Medians and rates were estimated by KM method. ‡HR and CI were estimated from a stratified Cox proportional hazards model. Model stratified by timing and outcome of cytoreductive surgery and geographical region. §P value from a stratified log rank test. 104 (with PFS rank) unstable.

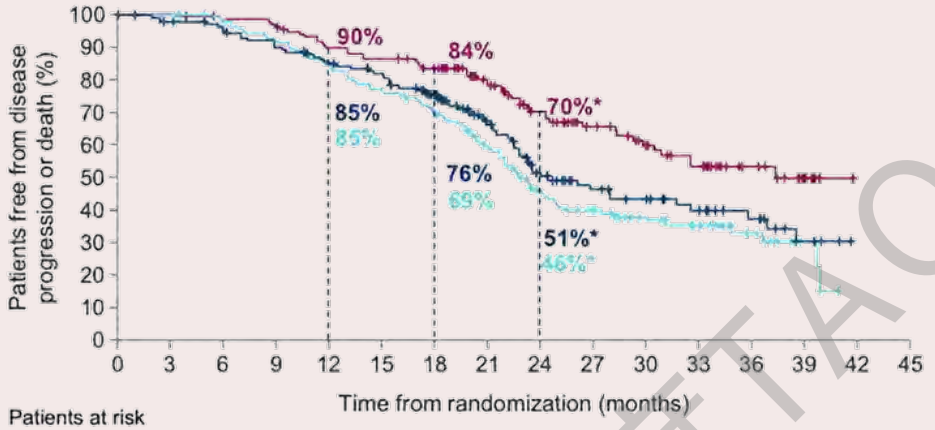
Harter P, Trillisch F, Okamoto A, et al: Durvalumab with paclitaxel/carboplatin and bevacizumab followed by maintenance durvalumab, bevacizumab and olaparib in patients with newly diagnosed advanced ovarian cancer without a tumor BRCA1/BRCA2 mutation: Results from the randomized, placebo-controlled phase III DUO-O/ENGOT-ov46/AGO-OVAR 23/GOG-3025 trial. 2023 ASCO Annual Meeting. Abstract LBA5506. Presented June 3, 2023.

Maintenance Therapy – PARPi + ICI

DUO-O

Subgroup analysis of PFS by HRD status

Non-tBRCAm HRD-positive

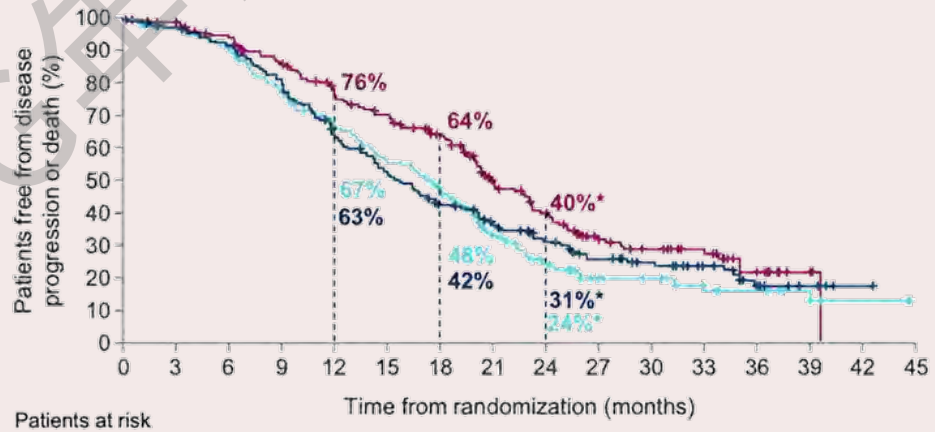


Patients at risk

Arm 1	143	141	136	126	116	105	93	73	52	41	31	22	13	6	0
Arm 2	148	142	137	128	118	112	94	66	45	34	28	21	15	7	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 2 PC + bev + durva N=148	Arm 3 PC + bev + durva + ola N=140
Events, n (%)	86 (60)	69 (47)	49 (35)
Median PFS, months†	23.0	24.4‡	37.3‡
HR (95% CI) vs Arm 1		**0.82** (0.60–1.12)§	**0.51** (0.36–0.72)§

HRD-negative



Patients at risk

Arm 1	216	203	188	159	135	112	92	55	34	21	19	12	9	5	2	0
Arm 2	199	189	177	153	120	97	76	59	45	33	25	17	8	4	1	0
Arm 3	211	202	190	169	145	132	111	75	57	33	26	20	10	3	0	

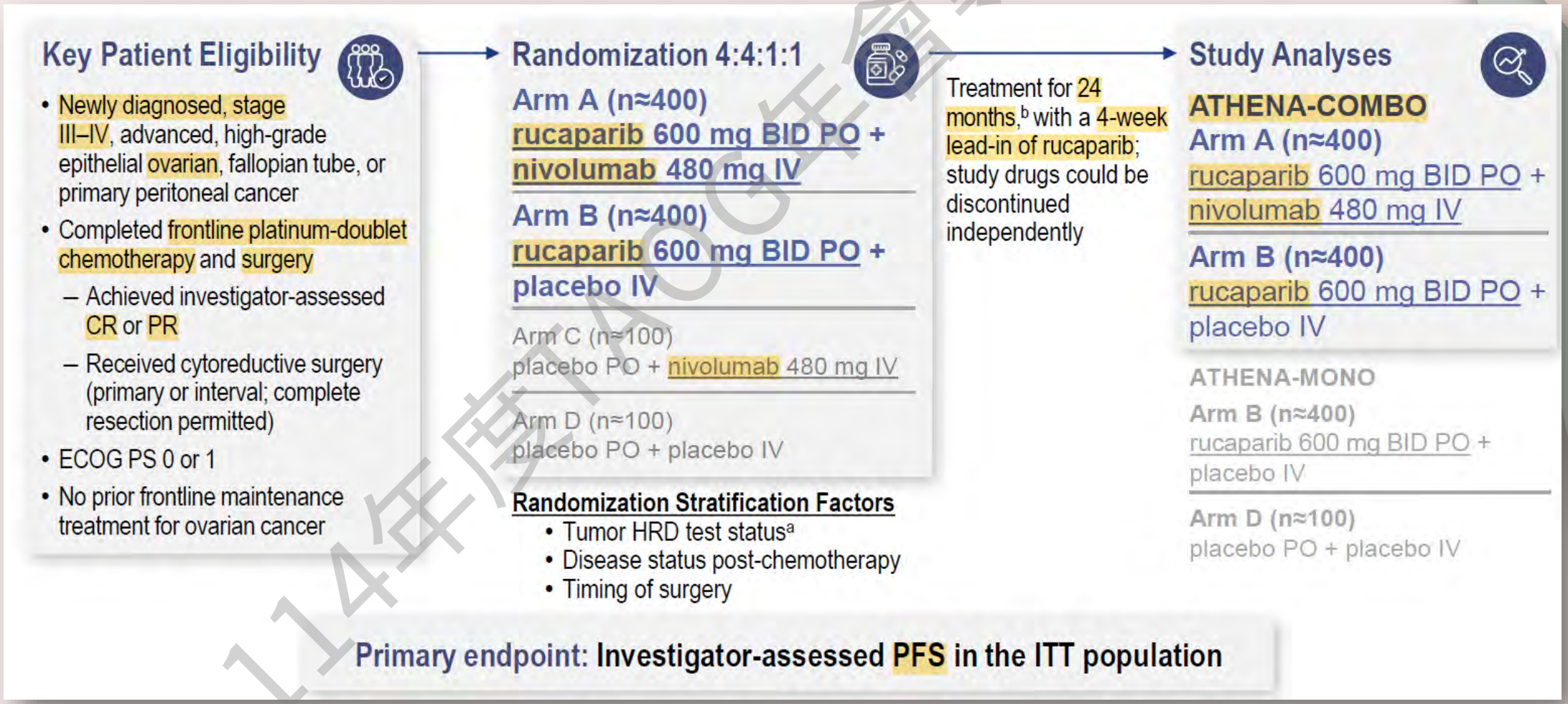
	Arm 1 PC + bev N=216	Arm 2 PC + bev + durva N=199	Arm 3 PC + bev + durva + ola N=211
Events, n (%)	157 (73)	142 (71)	127 (60)
Median PFS, months†	17.4	15.4	20.9
HR (95% CI) vs Arm 1		**0.94** (0.75–1.18)§	**0.68** (0.54–0.86)§

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

Harter P, Trillisch F, Okamoto A, et al: 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. 2023 ASCO Annual Meeting. Abstract LBA5506. Presented June 3, 2023.

Maintenance Therapy – PARPi + ICI

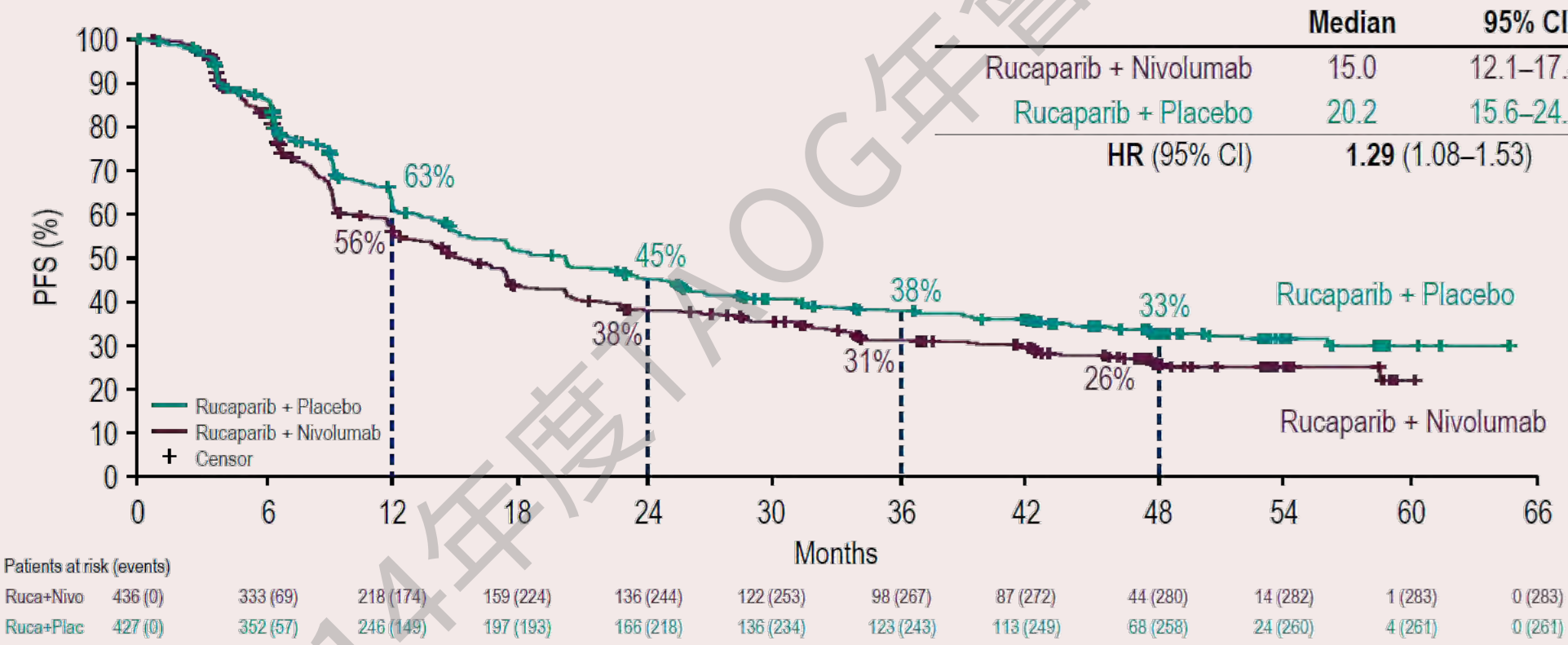
ATHENA - Combo



Monk, B.J. et al., LBA30 ATHENA-COMBO, a phase III, randomized trial comparing rucaparib (RUCA) + nivolumab (NIVO) combination therapy vs RUCA monotherapy as maintenance treatment in patients (pts) with newly diagnosed ovarian cancer (OC), Annals of Oncology, Volume 35, S1223 - S1224

Maintenance Therapy – PARPi + ICI

ATHENA - Combo



	Median	95% CI
Rucaparib + Nivolumab	15.0	12.1–17.4
Rucaparib + Placebo	20.2	15.6–24.0
HR (95% CI)	**1.29** (1.08–1.53)	

Patients at risk (events)

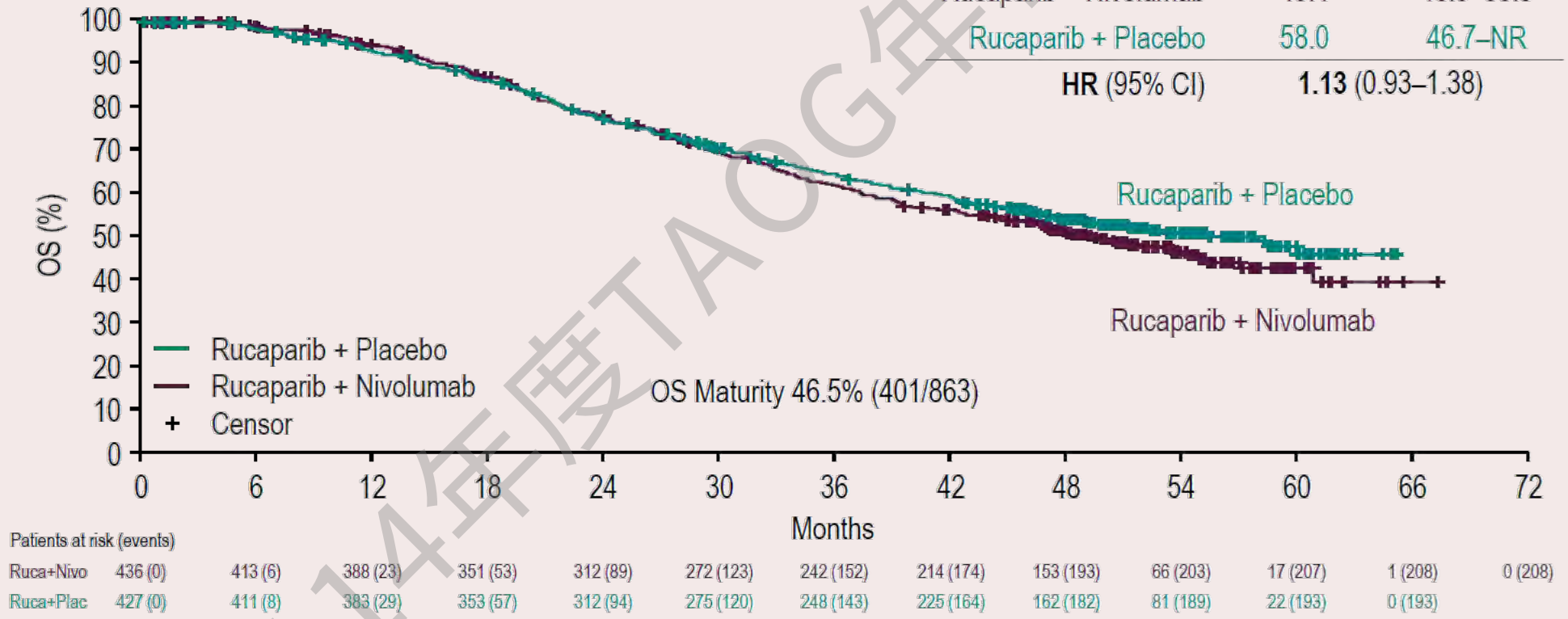
Ruca+Nivo	436 (0)	333 (69)	218 (174)	159 (224)	136 (244)	122 (253)	98 (267)	87 (272)	44 (280)	14 (282)	1 (283)	0 (283)
Ruca+Plac	427 (0)	352 (57)	246 (149)	197 (193)	166 (218)	136 (234)	123 (243)	113 (249)	68 (258)	24 (260)	4 (261)	0 (261)

Monk, B.J. et al., LBA30 ATHENA-COMBO, a phase III, randomized trial comparing rucaparib (RUCA) + nivolumab (NIVO) combination therapy vs RUCA monotherapy as maintenance treatment in patients (pts) with newly diagnosed ovarian cancer (OC), Annals of Oncology, Volume 35, S1223 - S1224

Maintenance Therapy – PARPi + ICI

ATHENA - Combo

	Median	95% CI
Rucaparib + Nivolumab	49.4	43.9–55.3
Rucaparib + Placebo	58.0	46.7–NR
HR (95% CI)	1.13 (0.93–1.38)	



Patients at risk (events)

Ruca+Nivo	436 (0)	413 (6)	388 (23)	351 (53)	312 (89)	272 (123)	242 (152)	214 (174)	153 (193)	66 (203)	17 (207)	1 (208)	0 (208)
Ruca+Plac	427 (0)	411 (8)	383 (29)	353 (57)	312 (94)	275 (120)	248 (143)	225 (164)	162 (182)	81 (189)	22 (193)	0 (193)	

Monk, B.J. et al., LBA30 ATHENA-COMBO, a phase III, randomized trial comparing rucaparib (RUCA) + nivolumab (NIVO) combination therapy vs RUCA monotherapy as maintenance treatment in patients (pts) with newly diagnosed ovarian cancer (OC), Annals of Oncology, Volume 35, S1223 - S1224

Maintenance Therapy – PARPi + ICI

ATHENA - Combo

COMBO vs MONO Data cutoff 17 May 2024

	RUCA + NIVO (COMBO), n	RUCA + PBO (MONO), n	Median investigator-assessed PFS, mo	HR (95% CI)
ITT	436	427	15.0 vs 20.2	1.3 (1.1–1.5)
HRD	193	185	28.9 vs 31.4	1.1 (0.9–1.5)
BRCA mutation	94	91	48.0 vs NR	1.1 (0.7–1.7)
BRCA wt/LOH^{high}	99	94	17.3 vs 22.3	1.1 (0.7–1.5)
BRCA wt/LOH^{low}	188	189	11.0 vs 12.1	1.3 (1.0–1.7)
BRCA wt/LOH^{indeterminate}	55	53	9.2 vs 17.5	1.6 (1.0–2.5)
PD-L1 ≥ 5%	69	72	22.8 vs 52.2	1.5 (0.9–2.4)
PD-L1 ≥ 1%	199	197	18.3 vs 25.8	1.3 (1.0–1.7)

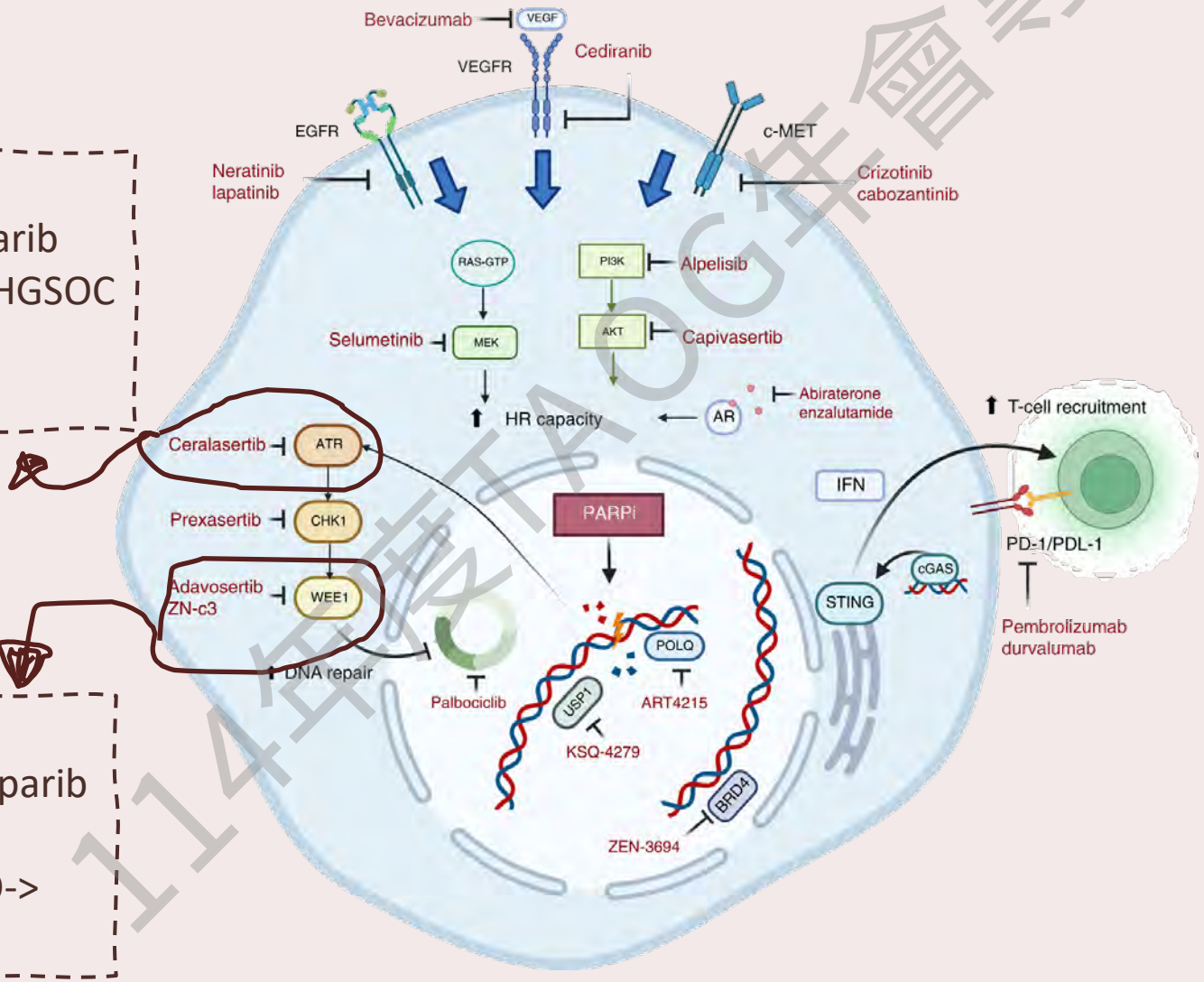
LOH, loss of heterozygosity; NR, not reached; wt, wild-type.

Monk, B.J. et al., LBA30 ATHENA-COMBO, a phase III, randomized trial comparing rucaparib (RUCA) + nivolumab (NIVO) combination therapy vs RUCA monotherapy as maintenance treatment in patients (pts) with newly diagnosed ovarian cancer (OC), Annals of Oncology, Volume 35, S1223 - S1224

Maintenance Therapy – PARPi Combination

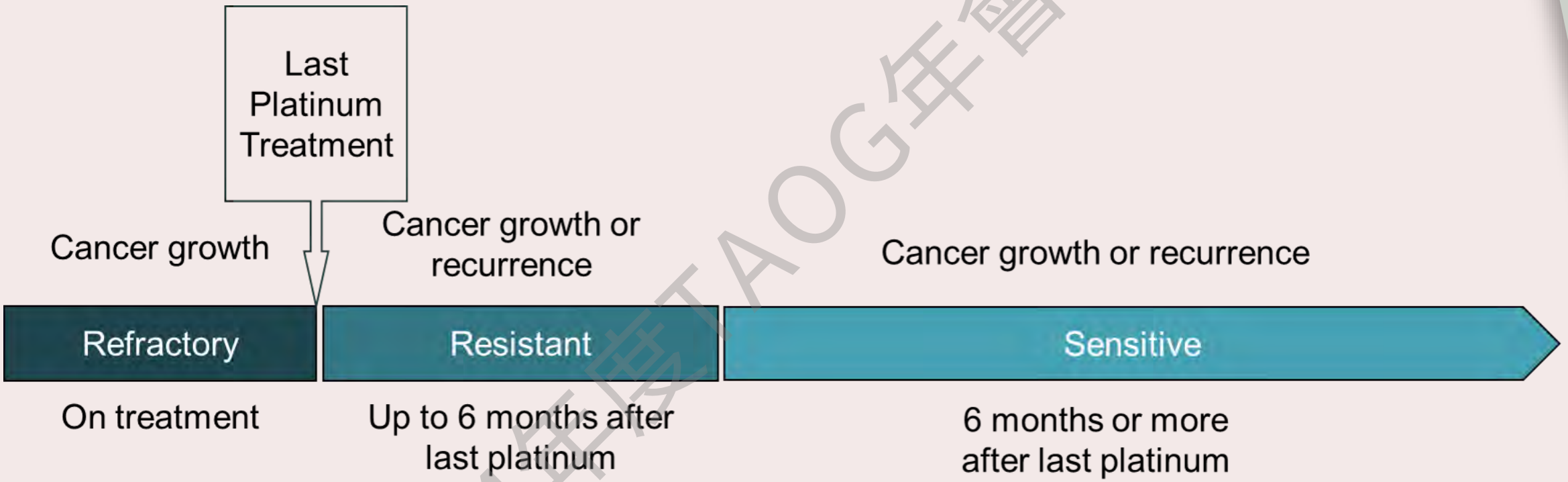
CAPRI trial
- ✓ Ceralasertib + Olaparib
- ✓ Platinum-sensitive HGSOC
- ✓ PARPi resistance
- ✓ ORR: about 50%

EFFORT trial
- ✓ Adavosertib +/- Olaparib
- ✓ PARPi resistance
- ✓ ORR: A-> 23% ; A+O-> 29%



Bhamidipati, D., Haro-Silerio, J.I., Yap, T.A. et al. PARP inhibitors: enhancing efficacy through rational combinations. Br J Cancer 129, 904–916 (2023). https://doi.org/10.1038/s41416-023-02326-7

Recurrence



https://www.avastin.com/hcp/ovar/efficacy-data.html

Platinum-sensitive

Recurrence - Treatment

Platinum-sensitive

- Consider secondary cytoreductive surgery
  - Should be to achieve residual disease that measures </= 0.5 cm
  - In patients who are able medically to tolerate a major surgical procedure

MSKCC criteria

DFI	Single Site	Multiple Sites: No Carcinomatosis	Carcinomatosis
6–12 Mo	Offer SC	Consider SC	No SC
12–30 Mo	Offer SC	Offer SC	Consider SC
>30 Mo	Offer SC	Offer SC	Offer SC

DFI: disease-free interval; Mo: months; SC: secondary cytoreduction.

Chi, D.S., et al. Guidelines and selection criteria for secondary cytoreductive surgery in patients with recurrent, platinum-sensitive epithelial ovarian carcinoma. Cancer, 106: 1933-1939.

Recurrence - Treatment

Platinum-sensitive

- Consider secondary cytoreductive surgery
  - DESKTOP III trial

AGO score

Predictive parameters of CGR
Platinum-sensitive ROC
Good performance status (ECOG 0)
No residual disease after primary surgery (or, alternatively, FIGO I/II)
Absence of ascites in preoperative imaging (<500 ml)

AGO, Arbeitsgemeinschaft Gynäkologische Onkologie; CGR, complete gross resection; ROC, recurrent ovarian cancer; FIGO, International Federation of Gynecology and Obstetrics; ECOG, Eastern Cooperative Oncology Group.

- ✓**Complete resection rate: 75.5%**
- ✓**mOS: surgery vs non-surgery 53.7m vs 46m (HR 0.75, p= 0.02)**

Harter P, et al. DESKTOP III Investigators. Randomized Trial of Cytoreductive Surgery for Relapsed Ovarian Cancer. N Engl J Med. 2021 Dec 2;385(23):2123-2131.

Recurrence - Treatment

Platinum-sensitive

- Platinum-based chemotherapy (+/- Bevacizumab)
  - Carboplatin + Paclitaxel
  - Carboplatin + Liposomal doxorubicin
  - Carboplatin + Gemcitabine

CALYPSOL

- ✓ **Randomized, Phase III**
- • **Platinum-sensitive recurrent Ov CA**
- ✓ **Carboplatin + Liposomal doxorubicin vs Carboplatin +Paclitaxel**
- ✓ **Results :**
- • **PFS: 9.4 m vs 8.8 m (HR 0.73, p= 0.004 for superiority)**
- • **OS: 30.7 m vs 33 m (HR 0.99, p= 0.94)**

Intergroup trial (the AGO-OVAR, the NCIC CTG, the EORTC GCG)

- ✓ **Randomized, Phase III**
- • **Platinum-sensitive recurrent Ov CA**
- ✓ **Carboplatin (AUC 4) + Gemcitabine (1000mg/m2) (D1, D8) vs Carboplatin (AUC 5)**
- ✓ **Results :**
- • **PFS: 8.6 m vs 5.8 m (HR 0.72, p= 0.0031)**
- • **OS: 18 m vs 17.3 m (HR 0.96)**
- • **ORR: 47.2% m vs 30.9% (p= 0.0016)**

Wagner U, et al. Final overall survival results of phase III GCIG CALYPSO trial of pegylated liposomal doxorubicin and carboplatin vs paclitaxel and carboplatin in platinum-sensitive ovarian cancer patients. Br J Cancer. 2012 Aug 7;107(4):588-91.

Pfisterer J, et al. Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG. J Clin Oncol. 2006 Oct 10;24(29):4699-707.

Recurrence - Treatment

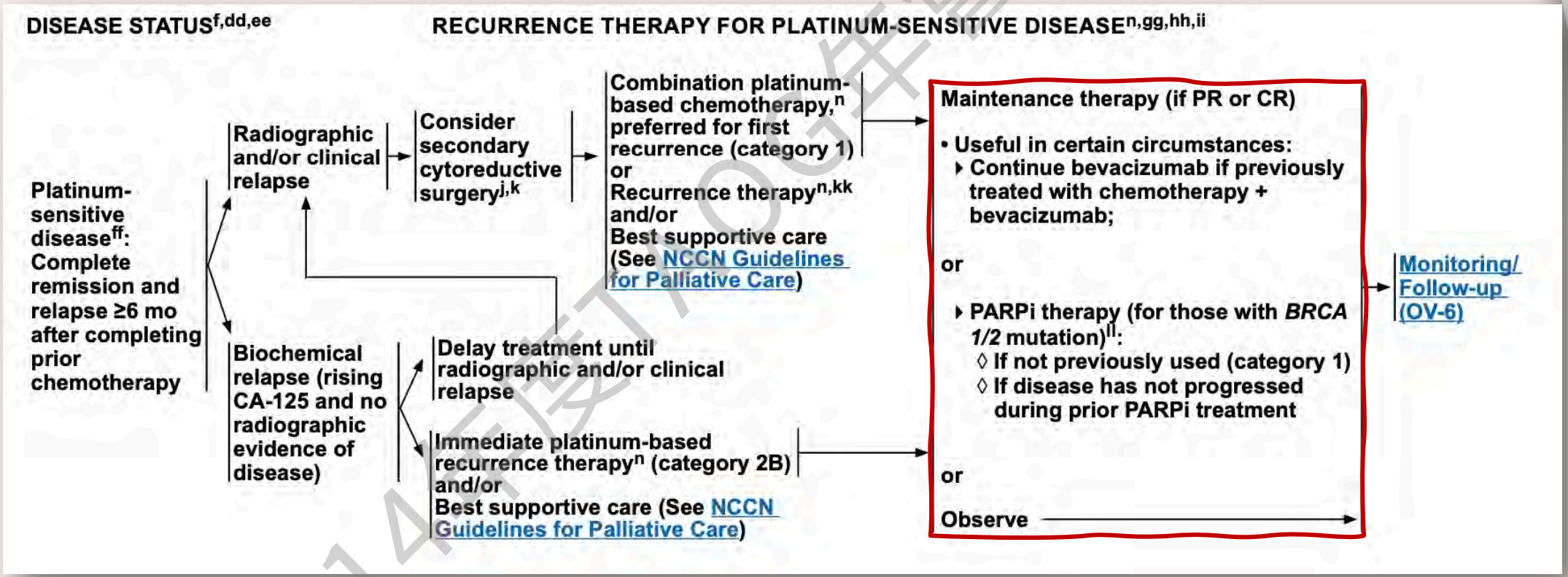
Platinum-sensitive

Recurrence Therapy for Platinum-Sensitive Disease[p] (alphabetical order)

Preferred Regimens	Other Recommended Regimens[s]		Useful in Certain Circumstances
Carboplatin/ gemcitabine[10] ± bevacizumab[i,q,r,11]	Carboplatin[t,10]	Ifosfamide	For mucinous carcinoma: • 5-FU/leucovorin/oxaliplatin ± bevacizumab (category 2B for bevacizumab)[i,q] • Capecitabine/oxaliplatin ± bevacizumab (category 2B for bevacizumab)[i,q]
Carboplatin/liposomal doxorubicin[12] ± bevacizumab[i,q,13]	Carboplatin/docetaxel[19, 20]	Irinotecan	Carboplatin/paclitaxel (for age >70)[f,t]
Carboplatin/paclitaxel[f,14] ± bevacizumab[i,q,r,15]	Carboplatin/paclitaxel (weekly)[f,21]	Melphalan	Carboplatin/paclitaxel, albumin bound (for confirmed taxane hypersensitivity)
Cisplatin/gemcitabine[16]	Capecitabine	Oxaliplatin	Irinotecan/cisplatin (for clear cell carcinoma)[27]
	Cisplatin[14]	Paclitaxel	Targeted Therapy
	Cyclophosphamide	Paclitaxel, albumin bound	Dabrafenib + trametinib (for *BRAF* V600E-positive tumors)[x,28]
	Doxorubicin	Pemetrexed	Entrectinib or larotrectinib (for *NTRK* gene fusion-positive tumors)[x]
		Vinorelbine	Selpercatinib (for *RET* gene fusion-positive tumors)[x,29]
Targeted Therapy (single agents)	Targeted Therapy		For low-grade serous carcinoma: • Trametinib[30] • Binimetinib (category 2B)[31,32]
Bevacizumab[i,q,17,18]	Niraparib/bevacizumab (category 2B)[i,22]		Hormone Therapy
	Niraparib (category 3)[u,23]		Fulvestrant (for low-grade serous carcinoma)
	Olaparib (category 3)[v,24]		Immunotherapy
	Pazopanib (category 2B)[25]		Dostarlimab-gxly (for dMMR/MSI-H recurrent or advanced tumors)[x,33]
	Rucaparib (category 3)[w,26]		Pembrolizumab (for MSI-H or dMMR solid tumors, or patients with TMB-H tumors ≥10 mutations/megabase)[x,34]
	Hormone Therapy		
	Aromatase inhibitors (anastrozole, exemestane, letrozole)		
	Leuprolide acetate		
	Megestrol acetate		
	Tamoxifen		

Recurrence - Treatment

Platinum-sensitive



NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. Version 1.2025

Recurrence - Treatment

Platinum-sensitive

Bevacizumab

OCEANS

- ✓ Randomized, Phase III
- Platinum-sensitive recurrent Ov CA
  - No prior treatment with Bevacizumab
- ✓ Carboplatin + Gemcitabine (D1, D8)
  Bevacizumab 15mg/kg, IV, Q3W
- ✓ Results :
- PFS: 12.4 m vs 8.4 m (HR 0.46)
- ORR: 78.4% vs 57.4% (p< 0.001)
  (mainly partial response)
- OS: 33.3 m vs 35.3 m
  (immature data)

GOG-0213

- ✓ Randomized, Phase III
- Platinum-sensitive recurrent Ov CA
  - Prior treatment with Bevacizumab: OK
- ✓ Carboplatin + Paclitaxel
  Bevacizumab 15mg/kg, IV, Q3W
- ✓ Results :
- OS: 42.2 m vs 37.3 m (HR 0.83)
- PFS: 13.8 m vs 10.4 m (HR 0.63)
- ORR: 78% m vs 59% (p< 0.0001)
  - Complete response: 32% vs 18%

Aghajanian C, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol. 2012 Jun 10;30(17):2039-45

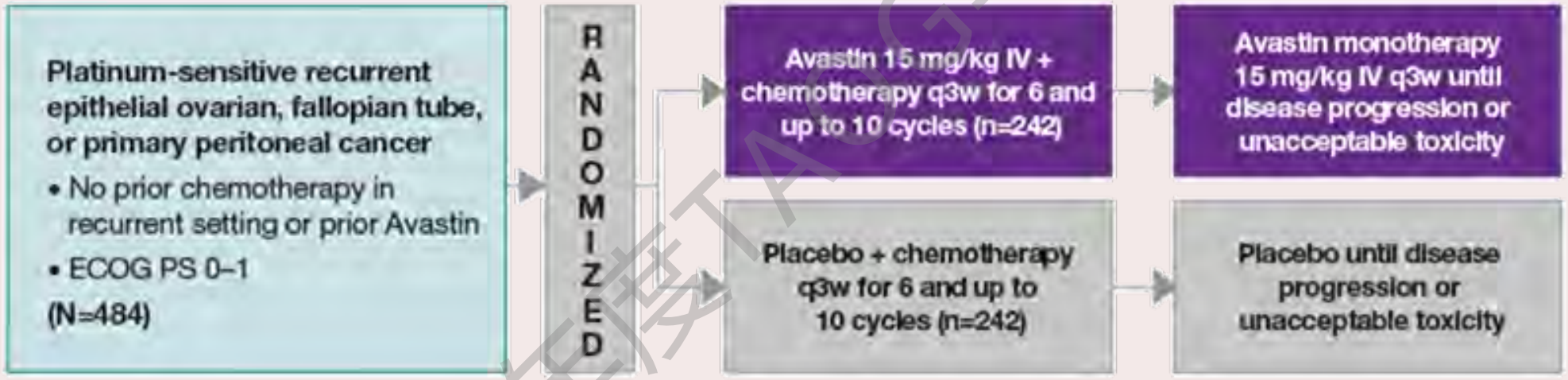
Coleman RL, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol. 2017 Jun;18(6):779-791

Recurrence - Treatment

Platinum-sensitive

Bevacizumab

OCEANS Trial



Main efficacy outcome measure: PFS
Secondary efficacy outcome measures: ORR, OS

Chemotherapy doses for both treatment arms:
• Carboplatin (AUC 4, Day 1) and gemcitabine (1000 mg/m^2 on Days 1 and 8) q3w

Aghajanian C, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol. 2012 Jun 10;30(17):2039-45

Recurrence - Treatment

Platinum-sensitive

Bevacizumab

OCEANS Trial

Baseline patient characteristics		
Age	Median age Range ≥65 years <65 years	61 years 28–87 years 37% 63%
ECOG PS	0 1 2	75% 24% <1%
Measurable disease	Measurable disease at baseline Baseline CA-125 levels above ULN (>35 U/mL)	100% 74%
Platinum-free interval	6–12 months >12 months	42% 58%

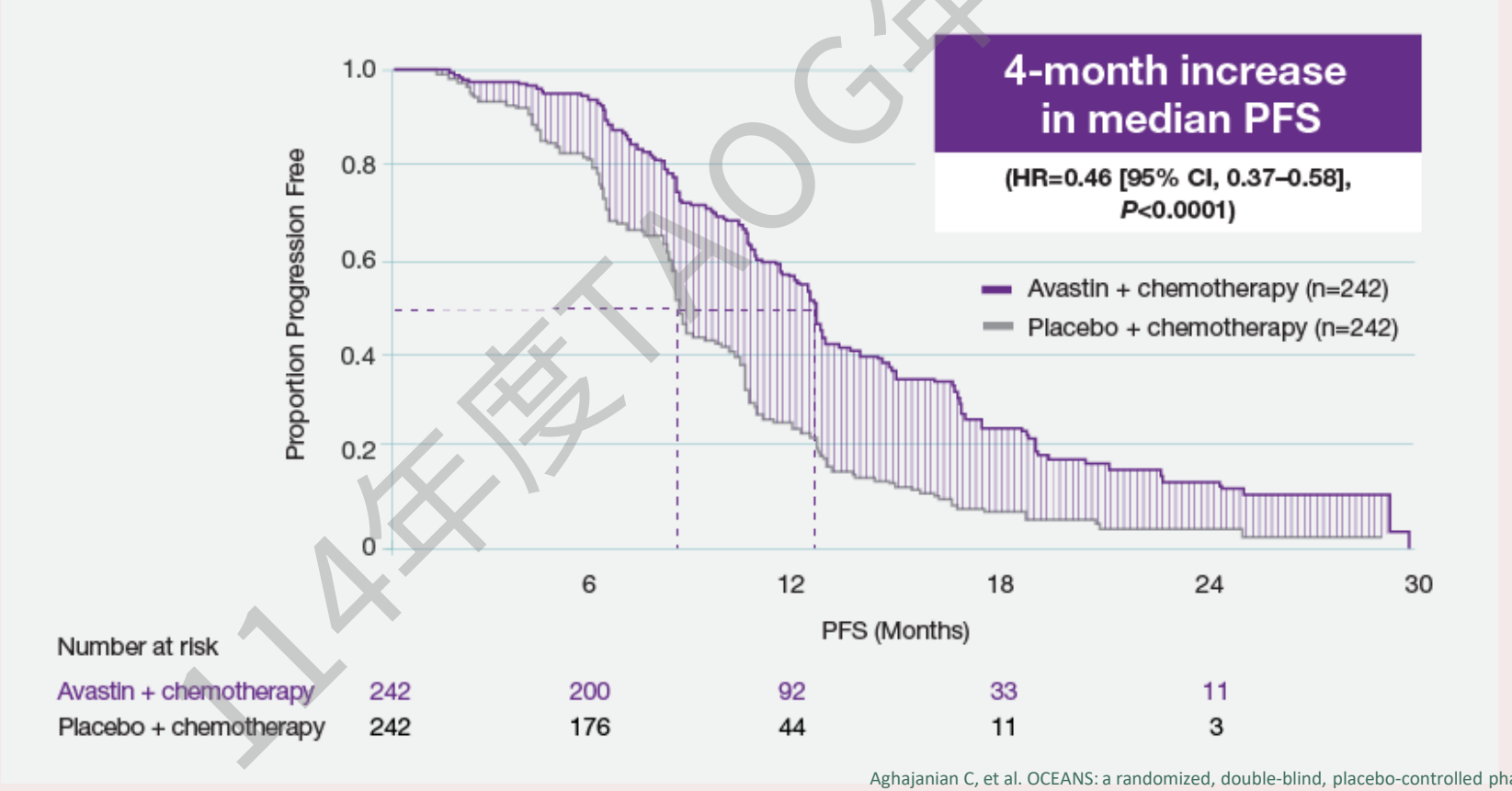
Aghajanian C, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol. 2012 Jun 10;30(17):2039-45

Recurrence - Treatment

Platinum-sensitive

Bevacizumab

OCEANS Trial



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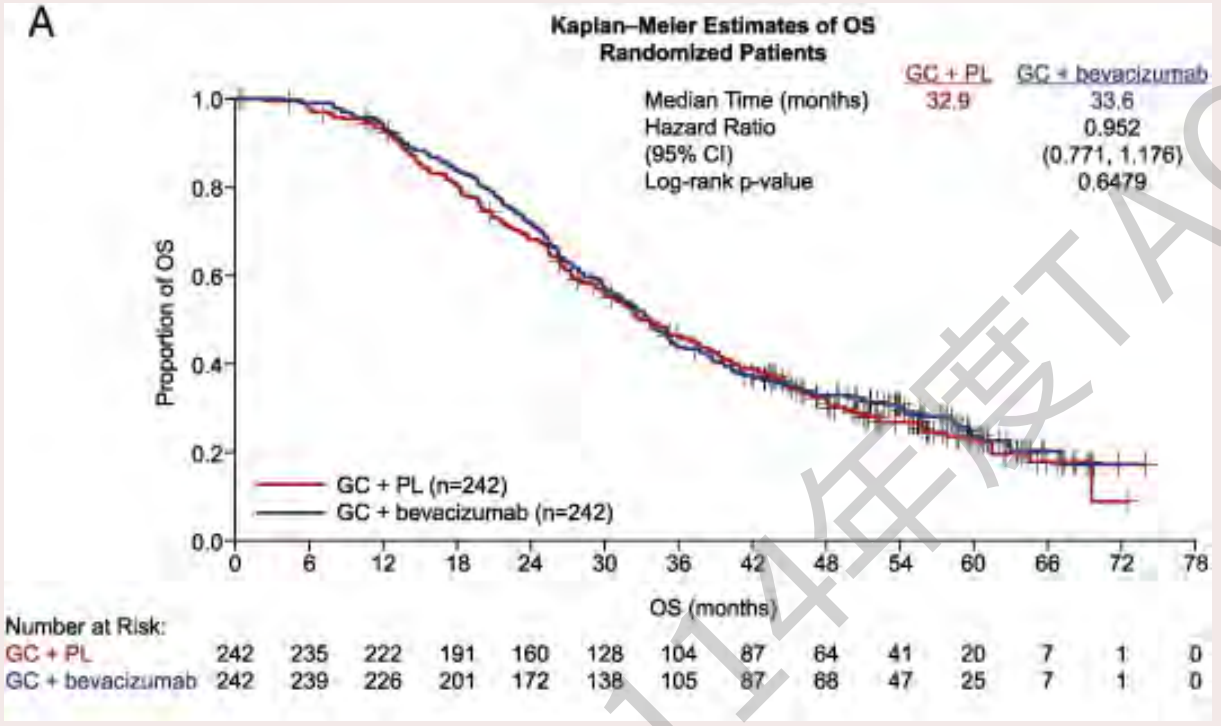
Recurrence - Treatment

Platinum-sensitive

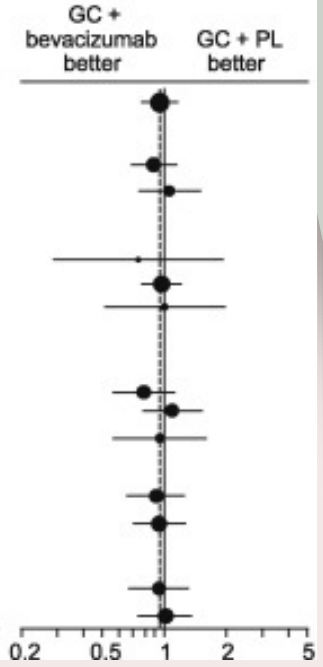
Bevacizumab

OCEANS Trial



B

Baseline risk factor	No. of patients	Median OS (mos) GC + PL (n=242)	Median OS (mos) GC + bevacizumab (n=242)	HR (95% CI)
All patients	484	32.9	33.6	0.95 (0.77–1.17)
Age, years				
<65	306	32.7	34.2	0.89 (0.69–1.16)
≥65	178	35.2	30.7	1.06 (0.75–1.50)
Primary site				
Fallopian tube carcinoma	29	43.1	49.9	0.75 (0.29–1.94)
Ovarian carcinoma	407	32.7	33.2	0.97 (0.77–1.21)
Primary peritoneal carcinoma	48	26.3	33.2	1.00 (0.51–1.98)
Recurrence since last platinum therapy				
<12 months	171	29.3	27.9	0.80 (0.57–1.11)
12–24 months	209	35.1	34.0	1.08 (0.79–1.49)
>24 months	104	50.8	43.1	0.95 (0.57–1.56)
Baseline SLD of target lesions				
≤Median (59.0)	244	38.7	40.3	0.91 (0.67–1.24)
>Median	240	29.3	30.4	0.94 (0.71–1.25)
Baseline CA125 (U/mL)				
≤Median (82.0)	232	39.3	40.3	0.94 (0.68–1.30)
>Median	226	29.1	26.6	1.01 (0.75–1.34)



Aghajanian C, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol. 2012 Jun 10;30(17):2039-45

Recurrence - Treatment

Platinum-sensitive

Bevacizumab

OCEANS Trial

Endpoint	Avastin + chemotherapy (n=242)	Placebo + chemotherapy (n=242)	HR (95% CI)	*P* value
PFS (main efficacy outcome measure)	12.4 months	8.4 months	0.46 (0.37–0.58)	<0.0001
ORR (secondary outcome measure)	78%	57%		<0.0001

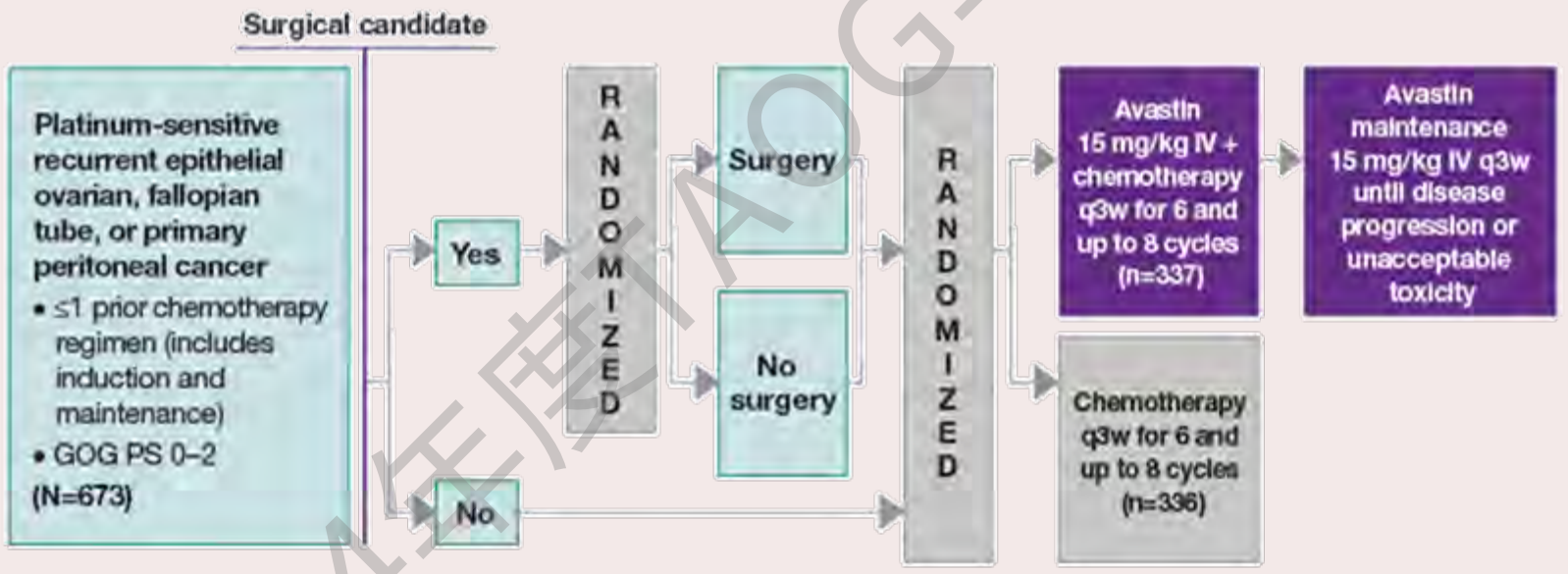
Aghajanian C, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol. 2012 Jun 10;30(17):2039-45

Recurrence - Treatment

Platinum-sensitive

Bevacizumab

GOG-0213



Main efficacy outcome measure: OS
Additional efficacy outcome measure: PFS
Exploratory efficacy outcome measure: ORR

Chemotherapy doses for both treatment arms:
• Carboplatin (AUC 5) and paclitaxel (175 mg/m² IV over 3 hours) q3w

Coleman RL, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol. 2017 Jun;18(6):779-791

Recurrence - Treatment

Platinum-sensitive

Bevacizumab

GOG-0213

Baseline patient characteristics		
Age	Median age Range ≥65 years <65 years	60 years 23–85 years 33% 67%
GOG PS	0 1 2	82% 17% 1%
Measurable disease	Measurable disease at baseline Baseline CA-125 levels above ULN (>35 U/mL)	83% 74%
Platinum-free interval	6–12 months >12 months	26% 74%

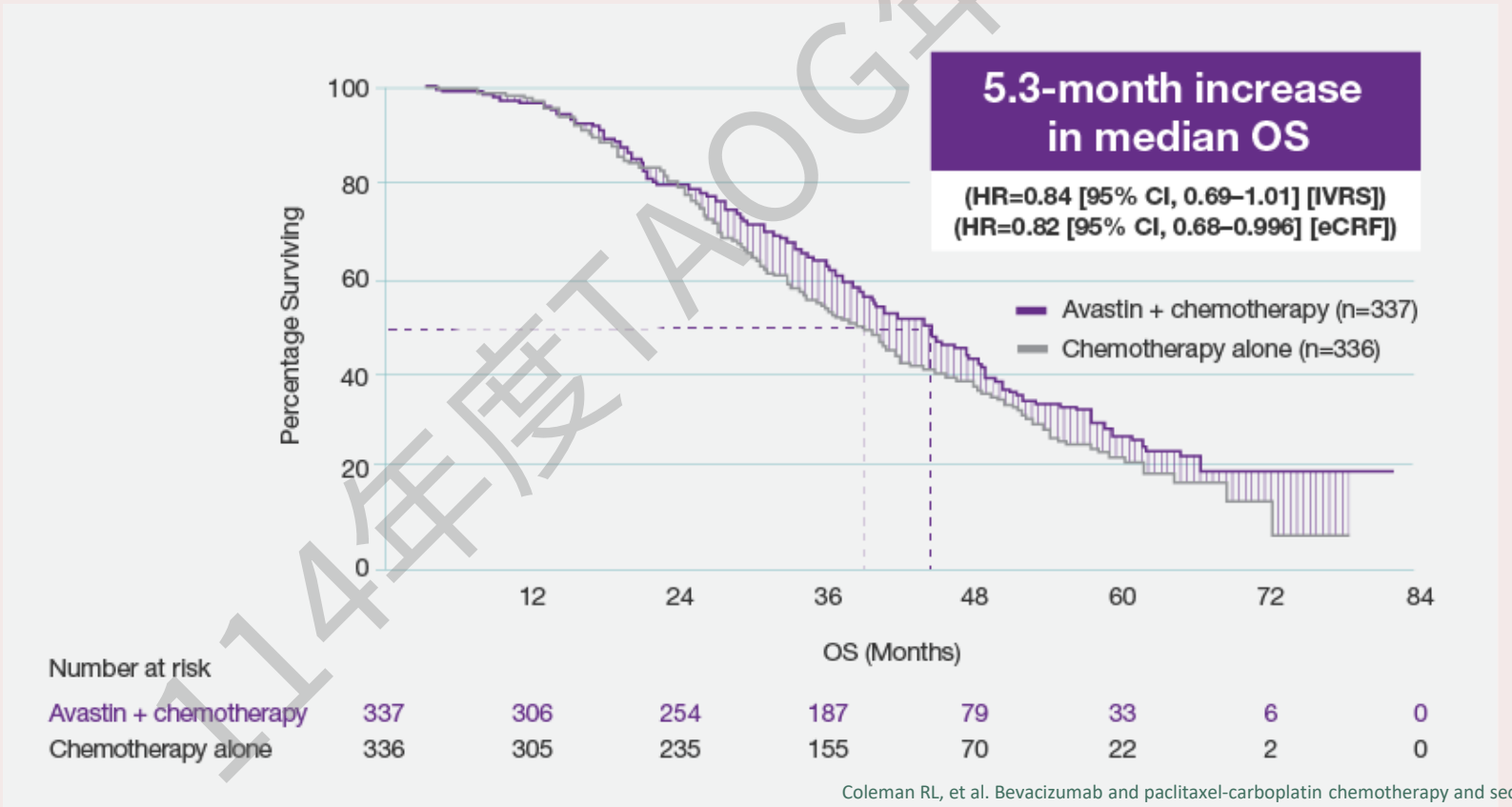
Coleman RL, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol. 2017 Jun;18(6):779-791

Recurrence - Treatment

Platinum-sensitive

Bevacizumab

GOG-0213



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Recurrence - Treatment

Platinum-sensitive

Bevacizumab

GOG-0213

Endpoint	Avastin + chemotherapy	Chemotherapy alone	HR (95% CI)
OS (main efficacy outcome measure)	42.6 months (n=337)	37.3 months (n=336)	0.84 (0.69–1.01 [IVRS]) 0.82 (0.68–0.996 [eCRF])
PFS (additional efficacy outcome measure)	13.8 months (n=337)	10.4 months (n=336)	0.61 (0.51–0.72 [IVRS])
ORR (exploratory efficacy outcome measure)	78% (n=274)*	56% (n=286)*	

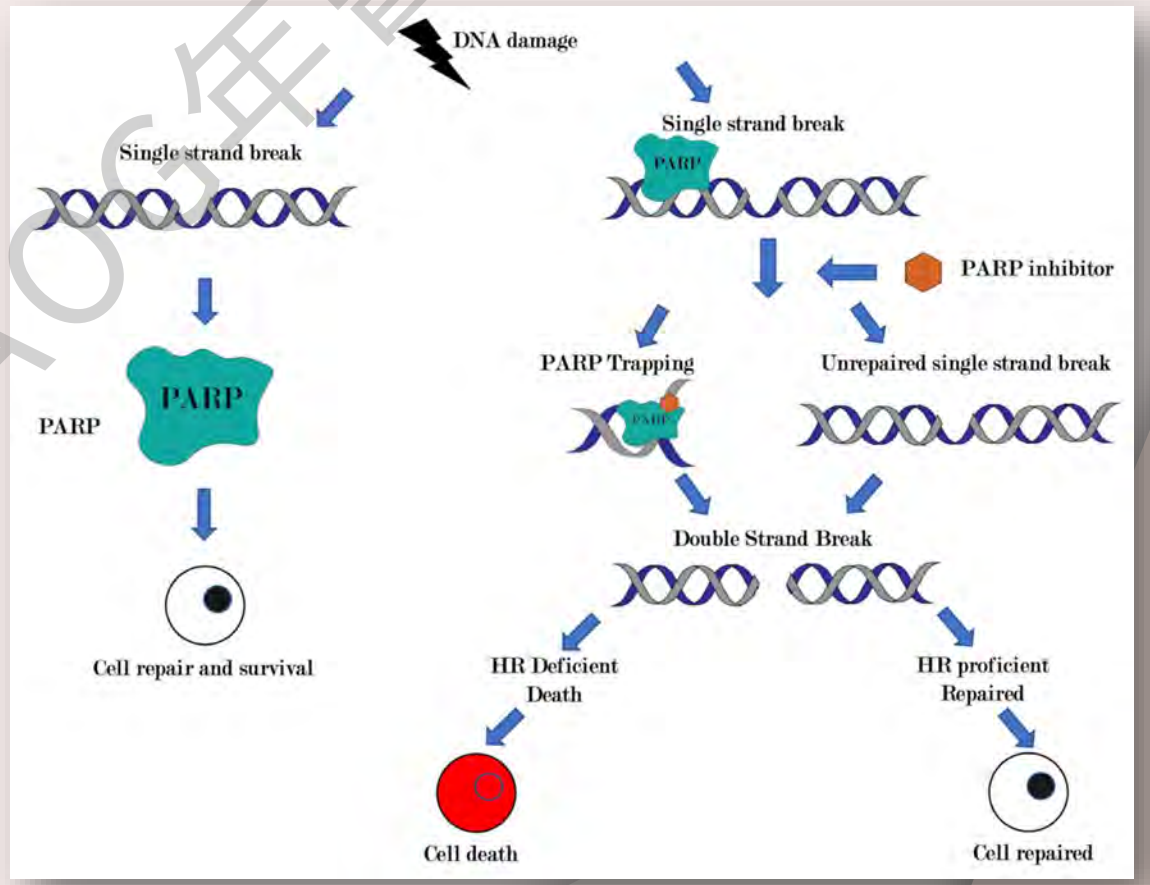
Coleman RL, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol. 2017 Jun;18(6):779-791

Recurrence - Treatment

Platinum-sensitive

PARPi

- Poly ADP-ribose polymerase inhibitor (PARPi):
  - Olaparib
  - Niraparib



Chan WY, Brown LJ, Reid L, Joshua AM. PARP Inhibitors in Melanoma—An Expanding Therapeutic Option? Cancers. 2021; 13(18):4520.

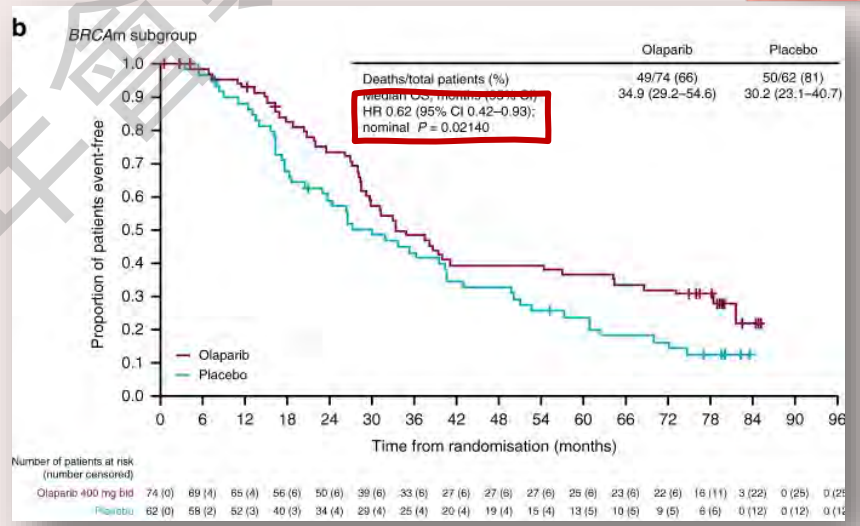
Recurrence - Treatment

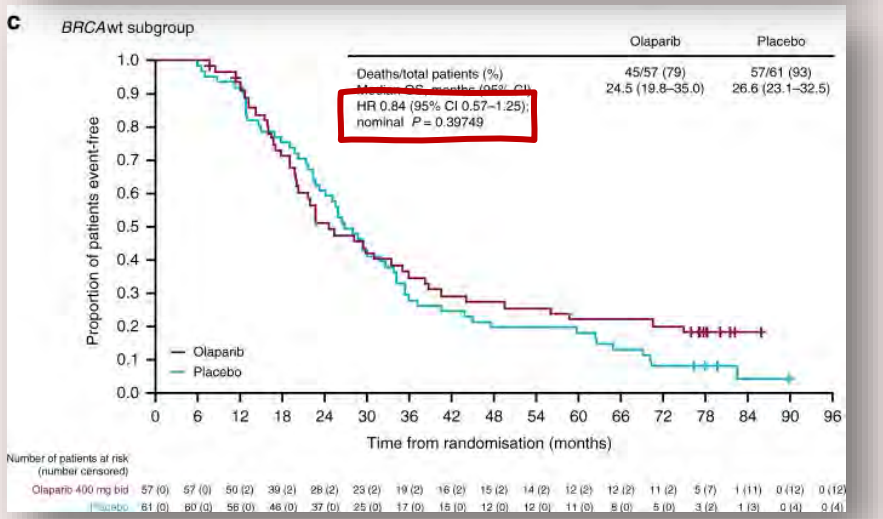
Platinum-sensitive

Olaparib

STUDY 19

- ✓ Randomized, Phase II
- Platinum-sensitive recurrent Ov CA
  - At least two platinum-based C/T -> CR or PR
- ✓ Maintenance Olaparib (400mg BID)
- ✓ Results :
- PFS: 8.4 m vs 4.8 m (HR 0.35) (p< 0.001)
- OS: 29.8 m vs 27.8 m (HR 0.73) (p=0.02138)





Friedlander, M., Matulonis, U., Gourley, C. et al. Long-term efficacy, tolerability and overall survival in patients with platinum-sensitive, recurrent high-grade serous ovarian cancer treated with maintenance olaparib capsules following response to chemotherapy. Br J Cancer 119, 1075–1085 (2018)

Recurrence - Treatment

Platinum-sensitive

Olaparib

SOLO-2

- ✓ Randomized, Phase III
- Platinum-sensitive recurrent Ov CA
  - BRCA ½ mutation
  - At least 2 lines of previous C/T
- ✓ Maintenance Olaparib (300mg BID)
- ✓ Results :
- PFS: 19.1 m vs 5.5 m (HR 0.3) (p< 0.0001)
- OS: 51.7 m vs 38.3 m (HR 0.74) (p= 0.054)

Poveda A, et al. Olaparib tablets as maintenance therapy in patients with platinum-sensitive relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): a final analysis of a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Oncol. 2021 May;22(5):620-631.

OPINION STUDY

- ✓ Randomized, Phase IIIb
- Platinum-sensitive recurrent Ov CA
  - Non germline BRCA ½ mutation
  - At least two platinum-based C/T
- ✓ Maintenance Olaparib (300mg BID)
- ✓ Results :
- PFS:
  - sBRCAm: 16.4m
  - HRD, including sBRCAm: 11.1m
  - HRD, excluding sBRCAm: 9.7 m
  - HRP: 7.3m

Poveda A, et al. Olaparib maintenance monotherapy in platinum-sensitive relapsed ovarian cancer patients without a germline BRCA1/BRCA2 mutation: OPINION primary analysis. Gynecol Oncol. 2022 Mar;164(3):498-504.

Recurrence - Treatment

Platinum-sensitive

Niraparib

NOVA trial

- ✓ Randomized, Phase III
- Platinum-sensitive recurrent Ov CA
  - At least 2 lines of previous C/T
- ✓ Maintenance Niraparib (300mg QD)
- ✓ Results :
- PFS:
  - gBRCAm: 21m vs 5.5m (HR 0.27)
  - HRD, excluding gBRCAm: 12.9m vs 3.8m (HR 0.38)
  - Overall non-gBRCAm: 9.3m vs 3.9m (HR 0.45)

Mirza MR, et al. ENGOT-OV16/NOVA Investigators. Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. N Engl J Med. 2016 Dec 1;375(22):2154-2164.

Overall survival

Cohort	Niraparib Maintenance	Placebo Maintenance	HR (95% CI)
Germline *BRCA*–mutated	40.9 months	38.1 months	0.85 (0.61–1.20)
Non–germline *BRCA*–mutated	31.0 months	34.8 months	1.06 (0.81–1.37)
Homologous repair–deficient	35.6 months	41.4 months	1.29 (0.85–1.95)
Homologous repair–proficient	27.9 months	27.9 months	0.93 (0.61–1.41)
Homologous repair not determined	29.8 months	20.2 months	0.62 (0.29–1.35)

CI = confidence interval; HR = hazard ratio.

Matulonis UA, Herrstedt J, Oza A, et al: Final overall survival and long-term safety in the ENGOT-OV16/NOVA phase III trial of niraparib in patients with recurrent ovarian cancer. Society of Gynecologic Oncology 2023 Annual Meeting on Women's Cancer. Presented March 25, 2023.

Platinum-resistant

Recurrence - Treatment

Platinum-resistant

DISEASE STATUS[e,cc,dd]	THERAPY FOR PERSISTENT DISEASE OR RECURRENCE[m,ff,gg,hh]
Platinum-resistant disease:[ee] Progression on primary, maintenance or recurrence therapy or Stable or persistent disease (if not on maintenance therapy) or Complete remission and relapse <6 mo after completing chemotherapy	→ Clinical trial[ii,jj] and/or Best supportive care (See NCCN Guidelines for Palliative Care) and/or Recurrence therapy (see OV-C, 9 of 11)[m,ii,kk]

Recurrence - Treatment

Platinum-resistant

- Single agent chemotherapy (+/- Bevacizumab)
- Response rate is similar
  - Topotecan: 20%
  - Gemcitabine: 19%
  - Liposomal doxorubicin: 26%
  - Oral etoposide: 27%.
  - Docetaxel: 22%
  - Weekly paclitaxel: 21%.

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. Version 1.2023 — December 22, 2022

Recurrence - Treatment

Platinum-resistant

Recurrence Therapy for Platinum-Resistant Disease (alphabetical order)

Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Cytotoxic Therapy Cyclophosphamide (oral)/ bevacizumab[i,35] Docetaxel[36] Etoposide, oral[37] Gemcitabine[38,39] Liposomal doxorubicin[38,39] Liposomal doxorubicin/ bevacizumab[i,q,40] Paclitaxel (weekly)[f,41] Paclitaxel (weekly)/ bevacizumab[f,i,q,40] Topotecan[42,43] Topotecan/bevacizumab[i,q,40] Targeted Therapy (single agents) Bevacizumab[i,q,17,18] Mirvetuximab soravtansine-gynx (for *FRα*-expressing tumors)[x,44]	Cytotoxic Therapy[s] Capecitabine Carboplatin[*] Carboplatin/docetaxel[*] Carboplatin/paclitaxel (weekly)[f,*] Carboplatin/gemcitabine[10] ± bevacizumab[i,q,r,11,*] Carboplatin/liposomal doxorubicin[12] ± bevacizumab[i,q,13,*] Carboplatin/paclitaxel[f,14] ± bevacizumab[i,q,r,15,*] Cyclophosphamide Doxorubicin Gemcitabine/cisplatin[16,*] Ifosfamide Irinotecan Ixabepilone/bevacizumab (category 2B)[i,y,46] Melphalan Oxaliplatin Paclitaxel Paclitaxel, albumin bound Pemetrexed Sorafenib/topotecan[45] Vinorelbine Targeted Therapy (single agents) Niraparib (category 3)[u,23] Olaparib (category 3)[v,24] Pazopanib (category 2B)[25] Rucaparib (category 3)[w,26] Hormone Therapy Aromatase inhibitors (anastrozole, exemestane, letrozole) Leuprolide acetate Megestrol acetate Tamoxifen	Carboplatin/paclitaxel (for age >70)[f,t,*] Carboplatin/paclitaxel, albumin bound (for confirmed taxane hypersensitivity)[*] Immunotherapy Dostarlimab-gxly (for dMMR/MSI-H recurrent or advanced tumors)[x,32] Pembrolizumab (for patients with MSI-H or dMMR solid tumors, or TMB-H tumors ≥10 mutations/ megabase)[x,33] Hormone Therapy Fulvestrant (for low-grade serous carcinoma) Targeted Therapy Dabrafenib + trametinib (for *BRAF* V600E-positive tumors)[x,28] Entrectinib or larotrectinib (for *NTRK* gene fusion positive tumors)[x] Mirvetuximab soravtansine-gynx/bevacizumab (for *FRα*-expressing tumors) (category 2B)[i,x,47, 48] Selpercatinib (for *RET* gene fusion-positive tumors)[x,29] For low-grade serous carcinoma: • Trametinib[30] • Binimetinib (category 2B)[31,32]

Recurrence - Treatment

Platinum-resistant

Bevacizumab

AURELIA

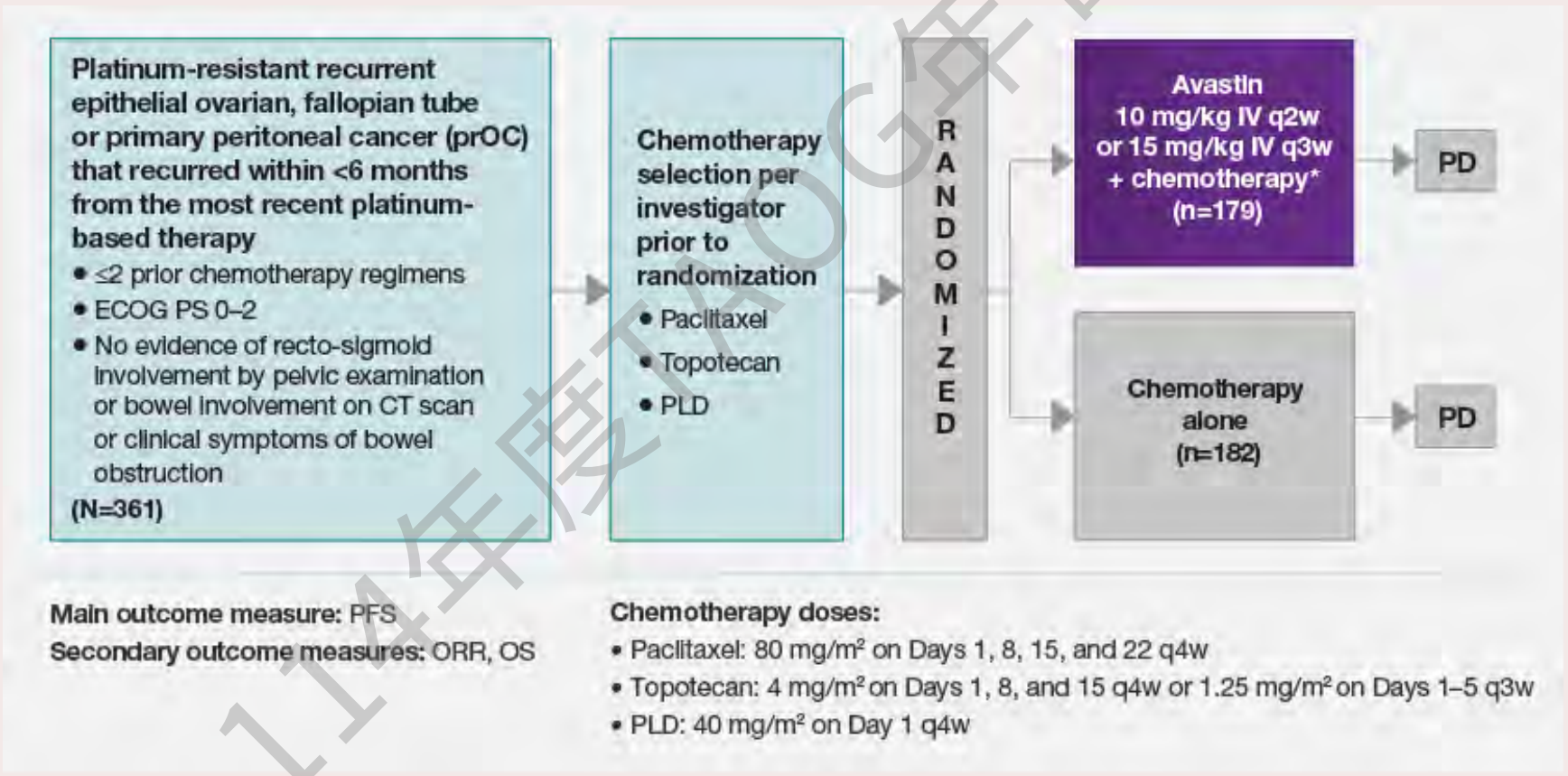
- ✓ Randomized, Phase III
- Platinum-resistant recurrent ovarian CA
- ✓ Weekly Paclitaxel/ Lipo-dox Q4W/ Weekly Topotecan/ Topotecan Q3W
  Bevacizumab 15mg/kg, IV, Q3W or 10mg/kg, IV, Q2W
- ✓ Results :
- PFS: 6.7 months vs 3.4 months (HR 0.38)
- ORR: 27.3% vs 11.8% (p< 0.001)
- OS: 16.6 months vs 13.3 months (HR 0.89)

Pujade-Lauraine E, etal: The AURELIA open-label randomized phase III trial. J Clin Oncol. 2014 May 1;32(13):1302-8. doi: 10.1200/JCO.2013.51.4489. Epub 2014 Mar 17. Erratum in: J Clin Oncol. 2014 Dec 10;32(35):4025. PMID: 24637997.

Recurrence - Treatment

Platinum-resistant

Bevacizumab



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Recurrence - Treatment

Platinum-resistant

Bevacizumab

The AURELIA study included a diverse population of women[1]

Baseline patient characteristics		
Age	Median age	61 years
	Range	25–84 years
	≥65 years	37%
	<65 years	63%
ECOG PS	0	59%
	1	34%
	2	7%
Baseline characteristics	Measurable disease at baseline	79%
	Baseline CA-125 levels ≥2 x ULN	87%
	Ascites at baseline	31%
Platinum-free interval	3–6 months	73%
	<3 months	27%

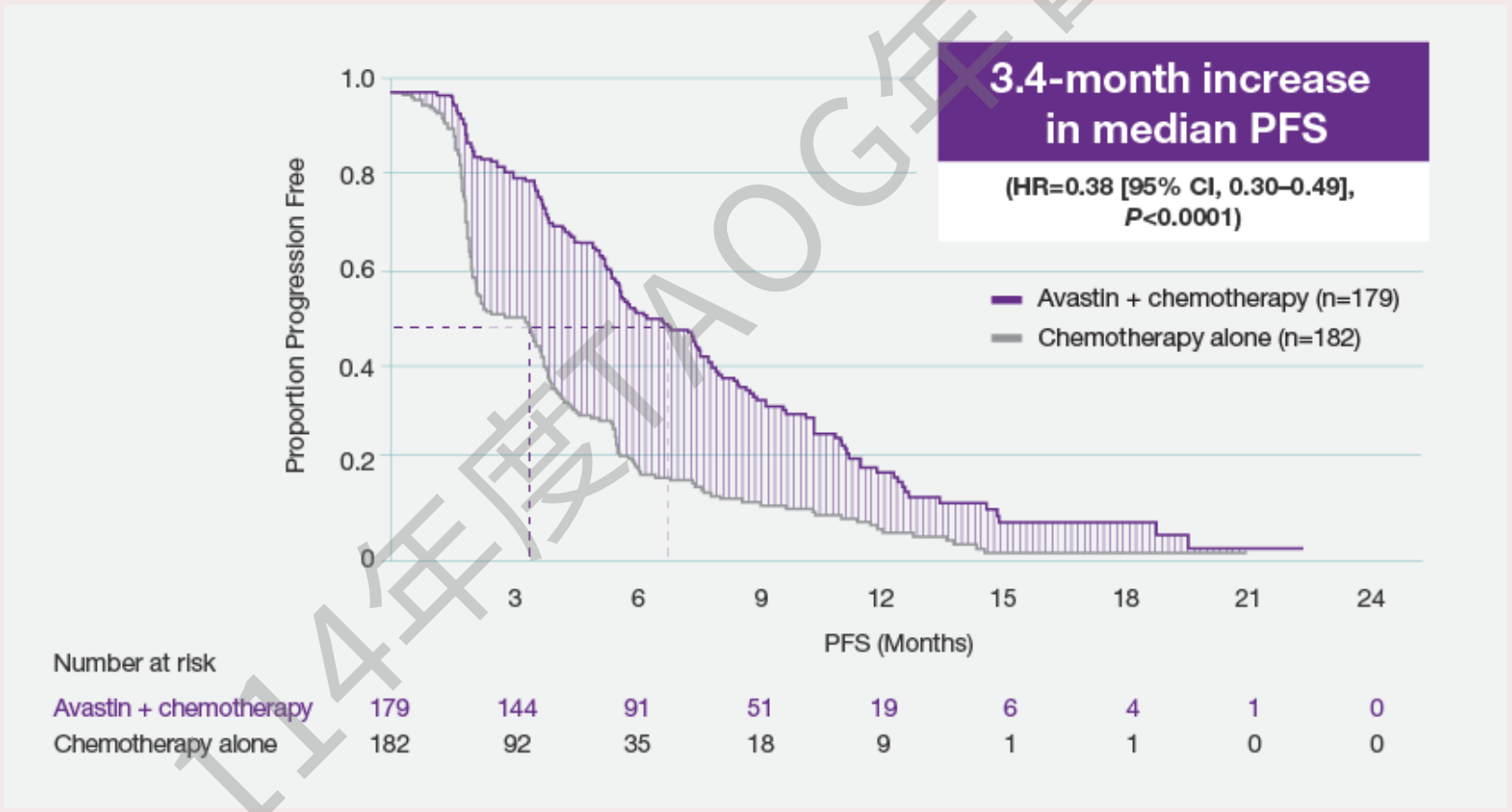
CA=cancer antigen; ULN=upper limit of normal.

Pujade-Lauraine E, etal: The AURELIA open-label randomized phase III trial. J Clin Oncol. 2014 May 1;32(13):1302-8. doi: 10.1200/JCO.2013.51.4489. Epub 2014 Mar 17. Erratum in: J Clin Oncol. 2014 Dec 10;32(35):4025. PMID: 24637997.

Recurrence - Treatment

Platinum-resistant

Bevacizumab



Pujade-Lauraine E, etal: The AURELIA open-label randomized phase III trial. J Clin Oncol. 2014 May 1;32(13):1302-8. doi: 10.1200/JCO.2013.51.4489. Epub 2014 Mar 17. Erratum in: J Clin Oncol. 2014 Dec 10;32(35):4025. PMID: 24637997.

Recurrence - Treatment

Platinum-resistant

Bevacizumab

AURELIA study: Efficacy data overview in ITT population[1]

Endpoint	Avastin + chemotherapy	Chemotherapy alone	HR (95% CI)	*P* value
PFS (main outcome measure)	6.8 months (n=179)	3.4 months (n=182)	0.38 (0.30–0.49)	<0.0001
OS (secondary outcome measure)	16.6 months (n=179) (95% CI, 13.7–19.0)	13.3 months (n=182) (95% CI, 11.9–16.4)	0.89 (0.69–1.14)	
ORR (secondary outcome measure)	28% (n=142) (95% CI, 21%–36%)	13% (n=144) (95% CI, 7%–18%)		

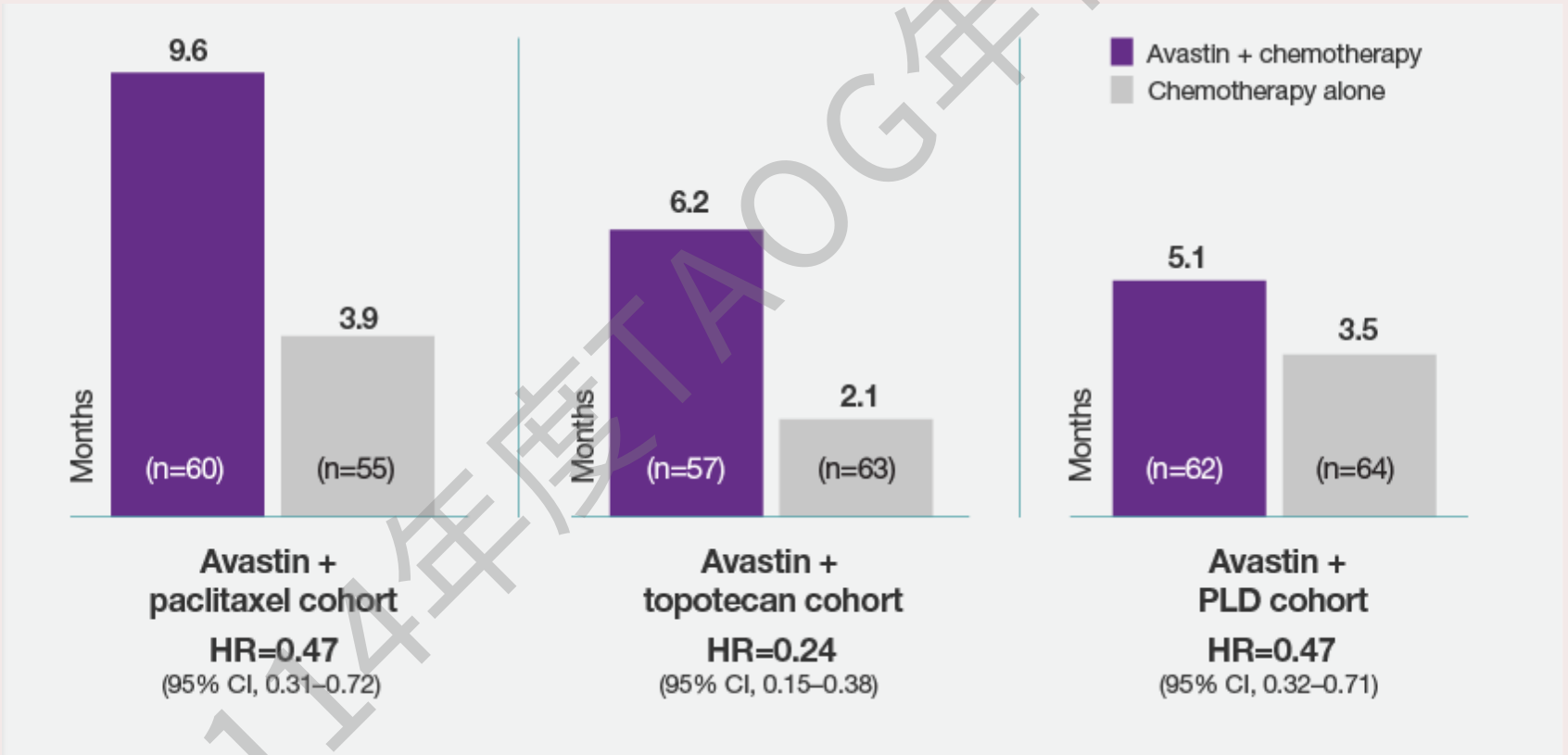
PFS=progression-free survival; HR=hazard ratio; CI=confidence interval; prOC=platinum-resistant ovarian cancer; ITT=intent-to-treat; OS=overall survival.

Pujade-Lauraine E, etal: The AURELIA open-label randomized phase III trial. J Clin Oncol. 2014 May 1;32(13):1302-8. doi: 10.1200/JCO.2013.51.4489. Epub 2014 Mar 17. Erratum in: J Clin Oncol. 2014 Dec 10;32(35):4025. PMID: 24637997.

Recurrence - Treatment

Platinum-resistant

Bevacizumab



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Recurrence - Treatment

Platinum-resistant

Bevacizumab

Cohort analysis was exploratory. Analysis not designed to evaluate statistical significance between treatment arms or compare among the 3 chemotherapy cohorts.

Median OS by chemotherapy cohort

Chemotherapy cohort	Avastin + chemotherapy	Chemotherapy alone	HR (95% CI)
Avastin + paclitaxel	22.4 months (n=60)	13.2 months (n=55)	0.64 (0.41–1.01)
Avastin + topotecan	13.8 months (n=57)	13.3 months (n=63)	1.12 (0.73–1.73)
Avastin + PLD	13.7 months (n=62)	14.1 months (n=64)	0.94 (0.63–1.42)

Cohort analysis was exploratory. Analysis not designed to evaluate statistical significance between treatment arms or compare among the 3 chemotherapy cohorts.

ORR by chemotherapy cohort

Chemotherapy cohort	Avastin + chemotherapy	Chemotherapy alone
Avastin + paclitaxel	53% (95% CI, 39%–68%) (n=45)	30% (95% CI, 17%–44%) (n=43)
Avastin + topotecan	17% (95% CI, 6%–28%) (n=46)	2% (95% CI, 0%–6%) (n=50)
Avastin + PLD	16% (95% CI, 6%–26%) (n=51)	8% (95% CI, 0%–15%) (n=51)

Cohort analysis was exploratory. Analysis not designed to evaluate statistical significance between treatment arm or compare among the 3 chemotherapy cohorts.

Pujade-Lauraine E, etal: The AURELIA open-label randomized phase III trial. J Clin Oncol. 2014 May 1;32(13):1302-8. doi: 10.1200/JCO.2013.51.4489. Epub 2014 Mar 17. Erratum in: J Clin Oncol. 2014 Dec 10;32(35):4025. PMID: 24637997.

Recurrence - Treatment

Platinum-resistant

Bevacizumab + oral Cyclophosphamide

- ✓ Retrospective study (2006-2010); Platinum-resistant recurrent ovarian CA
- ✓ Bevacizumab 10 mg/kg every 14 days and oral cyclophosphamide 50 mg daily
- ✓ Overall response rate: 42.4%; Median PFS: 5 m; Median OS: 20m

Barber EL, et al. The combination of intravenous bevacizumab and metronomic oral cyclophosphamide is an effective regimen for platinum-resistant recurrent ovarian cancer. J Gynecol Oncol. 2013 Jul;24(3):258-64.

- ✓ Retrospective study; Platinum-resistant recurrent ovarian CA
- ✓ Bevacizumab 10 mg/kg every 14 days and oral cyclophosphamide 50 mg daily
- ✓ Overall RR: CR 8.1%, PR 32.4%, SD 8.1%; Median PFS: 4.5m; Median OS: 10.7m

Sánchez-Muñoz A,et al. Bevacizumab plus low-dose metronomic oral cyclophosphamide in heavily pretreated patients with recurrent ovarian cancer. Oncology. 2010;79(1-2):98-104.

Recurrence - Treatment

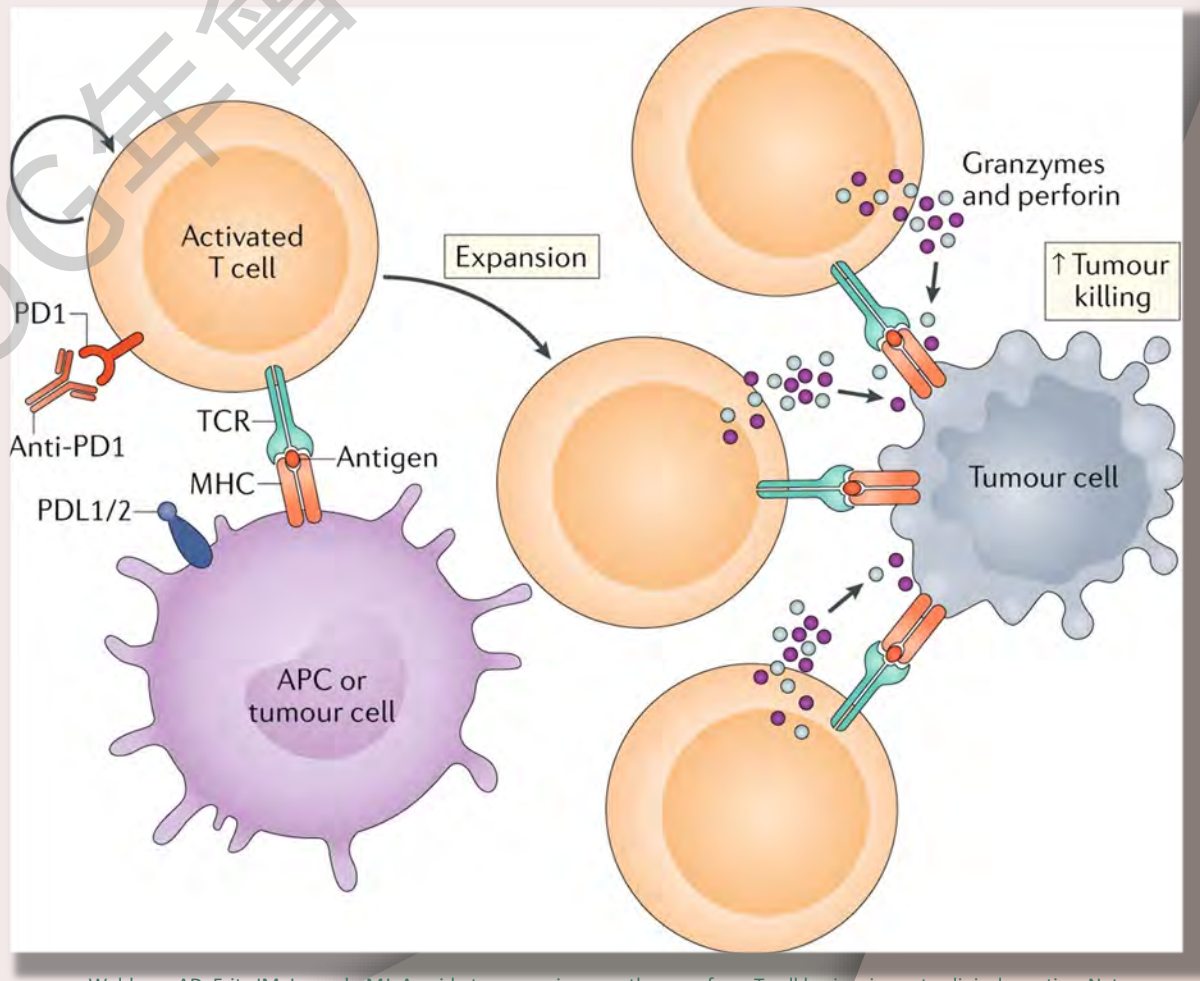
Platinum-resistant

Bevacizumab + Pembrolizumab + oral Cyclophosphamide

Recurrence - Treatment

Platinum-sensitive

- Immune Checkpoint Inhibitor
  - Anti-CTLA4
  - Anti- PD-1 antibody : ***Pembrolizumab***, Nivolumab, Dostarlimab
  - Anti-PD-L1 antibody: Avelumab, Durvalumab



Waldman AD, Fritz JM, Lenardo MJ. A guide to cancer immunotherapy: from T cell basic science to clinical practice. Nature reviews. Immunology. 2020 Nov;20(11):651-668. DOI: 10.1038/s41577-020-0306-5. PMID: 32433532; PMCID: PMC7238960.

Recurrence - Treatment

Platinum-resistant

Bevacizumab + Pembrolizumab + oral Cyclophosphamide

- ✓ Single-arm, phase 2 nonrandomized
- ✓ Recurrent ovarian CA, platinum-resistant: 75%, platinum-sensitive: 25%
- ✓ Bevacizumab 15 mg/kg + Pembrolizumab 200mg Q3W + oral cyclophosphamide 50mg daily
- ✓ Overall response rate: 47.5%; Median PFS: 10 m

Zsiros E, et al. Efficacy and Safety of Pembrolizumab in Combination With Bevacizumab and Oral Metronomic Cyclophosphamide in the Treatment of Recurrent Ovarian Cancer: A Phase 2 Nonrandomized Clinical Trial. JAMA Oncol. 2021;7(1):78–85.

Recurrence - Treatment

Platinum-resistant

Bevacizumab + Pembrolizumab + oral Cyclophosphamide

- ✓ Retrospective (2021-2022)
- ✓ Platinum-resistant recurrent ovarian CA (Heavily pre-treated-> 4-9 lines C/T)
- ✓ Bevacizumab + Pembrolizumab + oral cyclophosphamide
- ✓ Overall response rate: 13%; Median PFS: 3.5 m

Andrikopoulou A, et al. Pembrolizumab in combination with bevacizumab and oral cyclophosphamide in heavily pre-treated platinum-resistant ovarian cancer. Int J Gynecol Cancer. 2023 Apr 3;33(4):571-576.

Recurrence - Treatment

Platinum-resistant

Bevacizumab + Pembrolizumab + Lipodox

PemBOv trial:

- ✓ **Pembrolizumab plus bevacizumab with or without pegylated liposomal doxorubicin-based chemotherapy**
- ✓ **Platinum-resistant ovarian cancer**

	Cohort A n=6	Cohort B n=19	Cohort C n=19
PFS	2.1	4.7	4.8
95% CI	1.3 - NR	2.1 - 7.6	2.1 - 7.5
median Follow-up	21.1	7.9	17.8

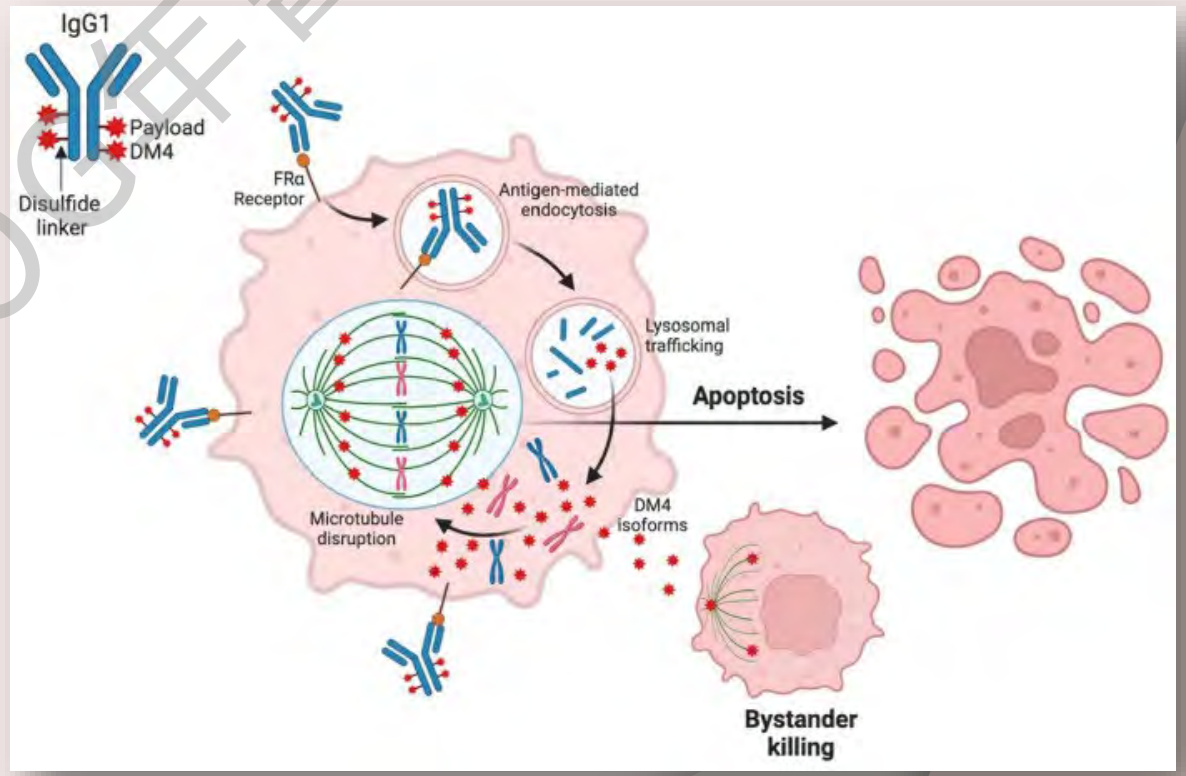
A: Pembrolizumab + Lipodox
B: Pembrolizumab + Bevacizumab
C: Pembrolizumab + Bevacizumab + Lipodox

Judith Michels, et al. PemBOv trial: Pembrolizumab plus bevacizumab with or without pegylated liposomal doxorubicin-based chemotherapy in patients with platinum-resistant ovarian cancer. Journal of Clinical Oncology 2022 40:16_suppl, 5575

Antibody Drug Conjugates

Antibody Drug Conjugates - MIRV

- Mirvetuximab soravtansine (MIRV, IMGN853)
  - Humanized FRα-binding monoclonal IgG1 antibody (M9346A)
  - Cytotoxic maytansinoid effector molecule DM4
  - Drug-to-antibody ratio: 3.5:1



Gonzalez-Ochoa E, Veneziani AC, Oza AM. Mirvetuximab Soravtansine in Platinum-Resistant Ovarian Cancer. Clin Med Insights Oncol. 2023 Jul 25;17:11795549231187264. doi: 10.1177/11795549231187264. PMID: 37528890; PMCID: PMC10387675.

Antibody Drug Conjugates - MIRV

SORAYA STUDY

- ✓ Single arm, Phase II
- Platinum-resistant recurrent Ov CA
  - Folate receptor α (FRα) high
  - 1-3 lines of prior therapy
- ✓ Mirvetuximab soravtansine (MIRV) 6 mg/kg IV Q3W
- ✓ Results :
- ORR: 32.4%
- mPFS: 4.3m
- mOS: 13.8m

MIRASOL STUDY

- ✓ Randomized, Phase III
- Platinum-resistant recurrent Ov CA
  - Folate receptor α (FRα) high
  - 1-3 lines of prior therapy
- ✓ MIRV 6 mg/kg IV Q3W vs C/T (Paclitaxel, Topotecan, Lipodox)
- ✓ Results :
- ORR: 42.3% vs 15.9% (p< 0.0001)
- PFS: 5.6 m vs 3.9 m (HR 0.65) (p< 0.0001)
- OS: 16.4 m vs 12.7 m (HR 0.67) (p= 0.046)

Ursula A, et al. Efficacy and Safety of Mirvetuximab Soravtansine in Patients With Platinum-Resistant Ovarian Cancer With High Folate Receptor Alpha Expression: Results From the SORAYA Study. Journal of Clinical Oncology 2023 41:13, 2436-2445

Kathleen N. Moore, et al. Phase III MIRASOL (GOG 3045/ENGOT-ov55) study: Initial report of 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 expression. Journal of Clinical Oncology 2023 41:17_suppl, LBA5507

Antibody Drug Conjugates - MIRV

MIRASOL STUDY

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.

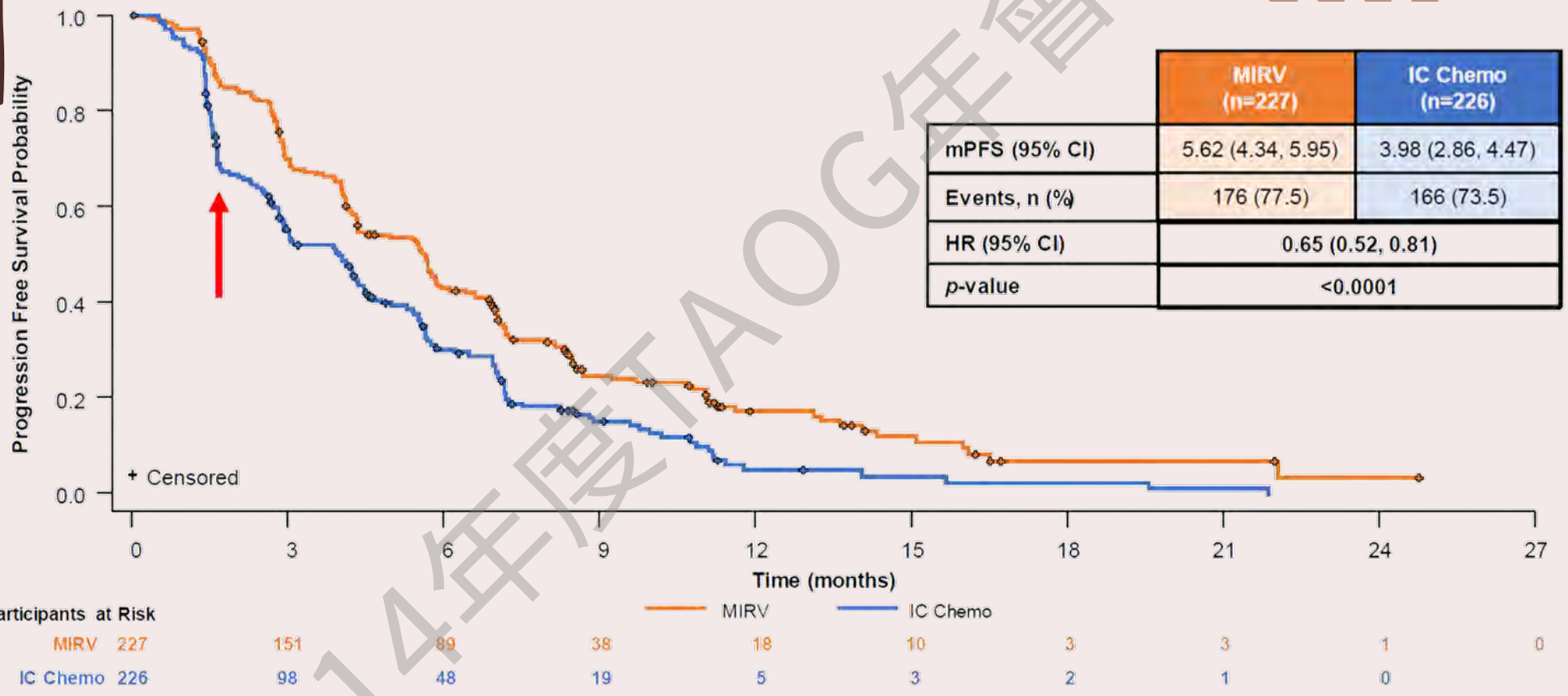
1. ClinicalTrials.gov identifier: NCT04209855. Updated June 16, 2022. Accessed October 5, 2022. https://clinicaltrials.gov/ct2/show/NCT04209855
2. Moore K, et al. Presented at: 2020 American Society of Clinical Oncology Annual Meeting; May 29-31, 2020; Virtual. Abstract TPS6103.

Kathleen N. Moore, et al. Phase III MIRASOL (GOG 3045/ENGOT-ov55) study: Initial report of 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 expression. Journal of Clinical Oncology 2023 41:17_suppl, LBA5507

Antibody Drug Conjugates - MIRV

MIRASOL STUDY

PFS



	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	

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.

Kathleen N. Moore, et al. Phase III MIRASOL (GOG 3045/ENGOT-ov55) study: Initial report of 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 expression. Journal of Clinical Oncology 2023 41:17_suppl, LBA5507

Antibody Drug Conjugates - MIRV

MIRASOL STUDY

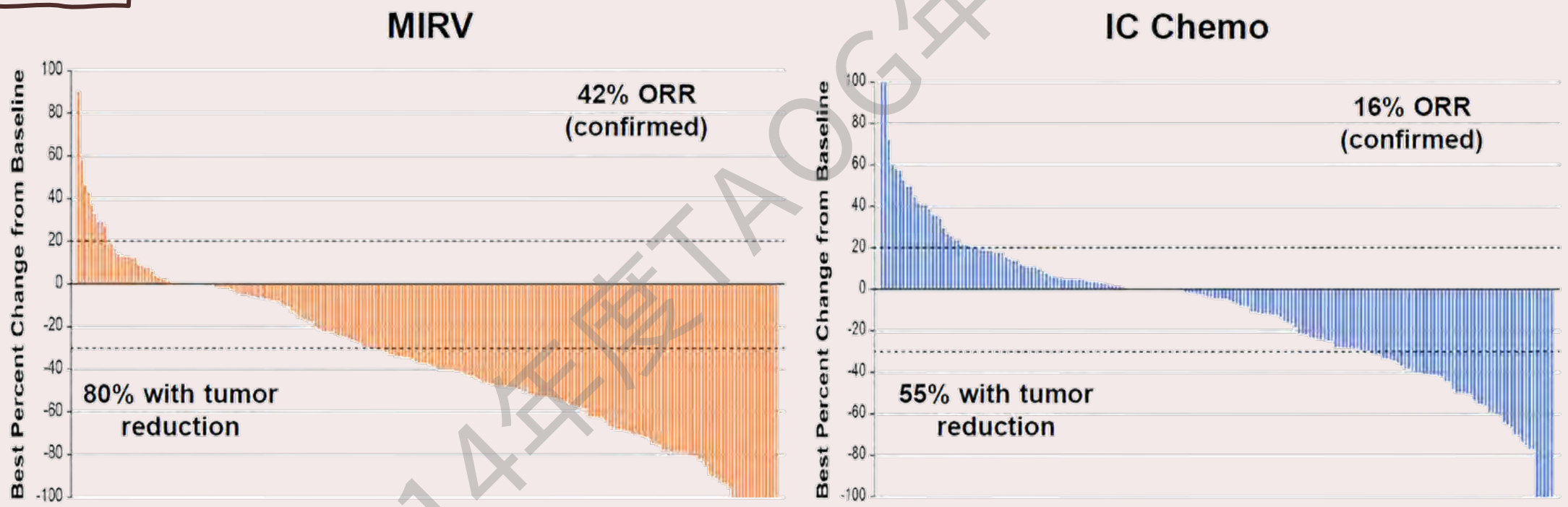
Objective response rate

	MIRV (n=227)	IC chemotherapy (n=226)
ORR (n. 95% CI)	42% (96, (35.8, 49.0))	16% (36, (11.4, 21.4))
Compete response (n, %)	12 (5%)	0
Partial response (n, %)	84 (37%)	36 (16%)
Stable disease (n, %)	86 (38%)	91 (40%)
Progressive disease (n, %)	31 (14%)	62 (27%)
Not evaluable (n, %)	14 (6%)	37 (16%)
	ORR difference: 26.4% (18.4, 34.4); p< 0.0001	

Kathleen N. Moore, et al. Phase III MIRASOL (GOG 3045/ENGOT-ov55) study: Initial report of 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 expression. Journal of Clinical Oncology 2023 41:17_suppl, LBA5507

Antibody Drug Conjugates - MIRV

MIRASOL STUDY

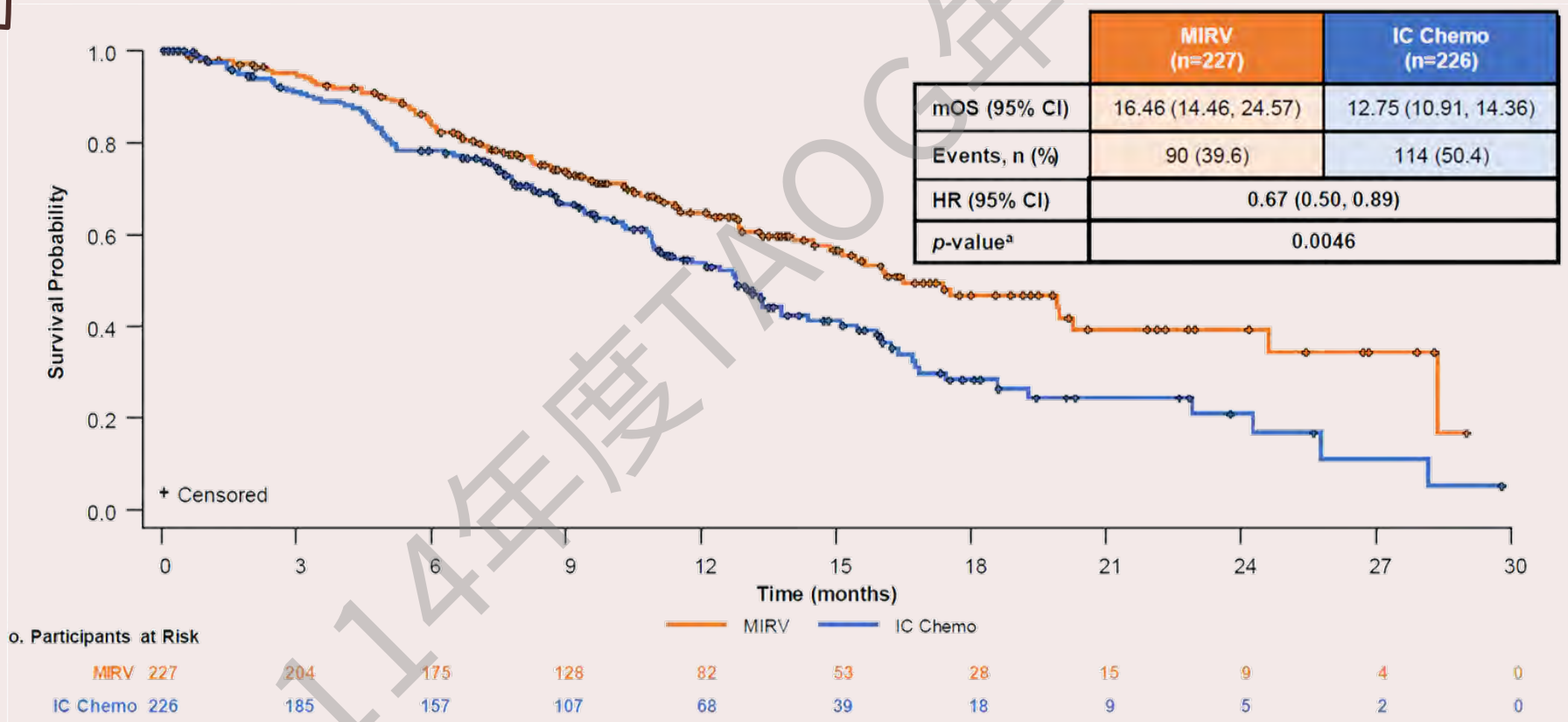


Kathleen N. Moore, et al. Phase III MIRASOL (GOG 3045/ENGOT-ov55) study: Initial report of mirvetuximab soravtansine vs. investigator's choice of chemotherapy in platinum-resistant, advanced high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high folate receptor-alpha expression. Journal of Clinical Oncology 2023 41:17_suppl, LBA5507

Antibody Drug Conjugates - MIRV

MIRASOL STUDY

OS



	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	

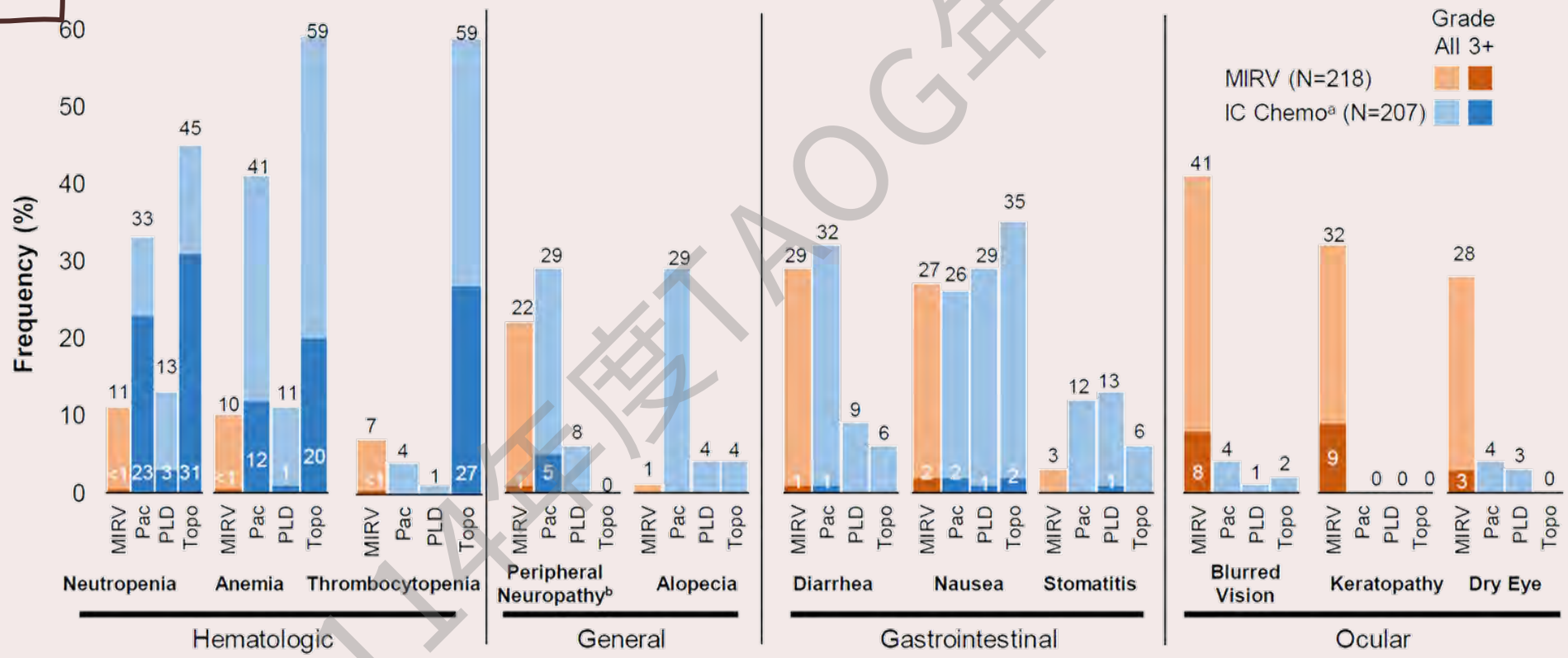
Data cutoff: March 6, 2023; median follow-up time: 13.11 months
MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mOS, median overall survival; CI, confidence interval; HR, hazard ratio.
[a]Overall survival is statistically significant based on pre-specified boundary p-value at interim analysis = 0.01313

Kathleen N. Moore, et al. Phase III MIRASOL (GOG 3045/ENGOT-ov55) study: Initial report of 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 expression. Journal of Clinical Oncology 2023 41:17_suppl, LBA5507

Antibody Drug Conjugates - MIRV

MIRASOL STUDY

Adverse Events



Data cutoff: March 6, 2023

MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; Pac, paclitaxel; PLD, pegylated liposomal doxorubicin; Topo, topotecan.

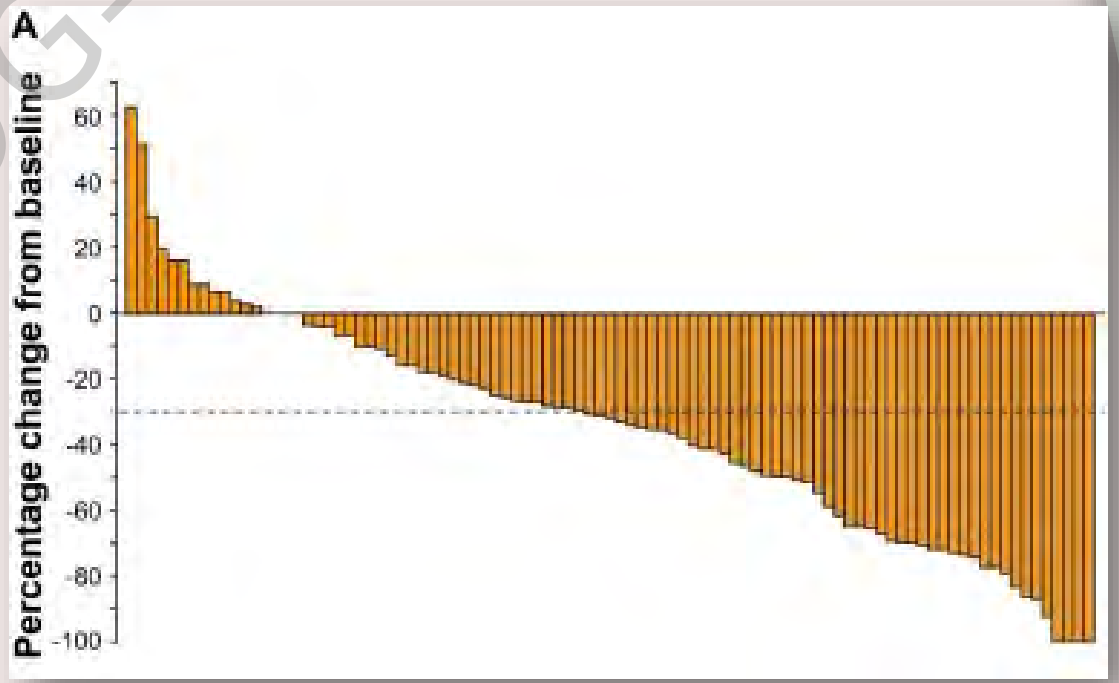
[a]Pac n=82 (39%), PLD n=76 (37%), Topo n=49 (24%). [b]Grade 2+ peripheral neuropathy events were observed in 12% and 16% of patients that received MIRV or paclitaxel, respectively.

Kathleen N. Moore, et al. Phase III MIRASOL (GOG 3045/ENGOT-ov55) study: Initial report of 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 expression. Journal of Clinical Oncology 2023 41:17_suppl, LBA5507

Antibody Drug Conjugates - MIRV

FORWARD II STUDY

- ✓ **Multi-arm, Phase Ib-II**
- **Platinum-resistant recurrent Ov CA**
  - **Folate receptor α (FRα) PS score ≥ 2+**
  - **1-3 lines of prior therapy**
- ✓ **Mirvetuximab soravtansine (MIRV) 6 mg/kg + *Bevacizumab* 15mg/kg IV Q3W**
- ✓ **Results :**
- **ORR: overall 44%; FRα high 48%**
- **mPFS: overall 8.2m; FRα high 9.7m**



Gilbert L, et al. Safety and efficacy of mirvetuximab soravtansine, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), in combination with bevacizumab in patients with platinum-resistant ovarian cancer. Gynecol Oncol. 2023 Mar;170:241-247. doi: 10.1016/j.ygyno.2023.01.020. Epub 2023 Feb 1. PMID: 36736157.

Antibody Drug Conjugates - MIRV

PICCOLO TRIAL

PICCOLO (NCT05041257) – Study Design[1-3]

BARCELONA 2024 ESMO congress

A single-arm, open-label, phase 2 trial of MIRV in patients with ≥3L platinum-sensitive ovarian cancer with FRα-high expression

PICCOLO Patient Population (N=79)

Enrollment and Key Eligibility

- Platinum-sensitive disease (defined as radiographic progression >6 months from last dose of most recent platinum therapy)
- FRα detected by IHC with PS2+ intensity among ≥75% of viable tumor cells[a]
- At least 2 prior platinum-containing regimens[b]
- Prior PARPi required if *BRCA*+
- Prior BEV not required
- Appropriate for single-agent therapy

→

Treatment Regimen

MIRV
(6 mg/kg AIBW Q3W)

Primary Endpoint

ORR by INV

Key Secondary Endpoint

DOR by INV

Other Secondary Endpoints

- Safety and tolerability
- CA-125 response (GCIG criteria)
- PFS
- OS
- Sensitivity analyses[c]

Mirvetuximab Soravtansine (MIRV) in Recurrent Platinum-Sensitive Ovarian Cancer (PSOC) with High Folate Receptor-Alpha (FRα) Expression: Results From the Phase II PICCOLO Trial (ESMO 2024)

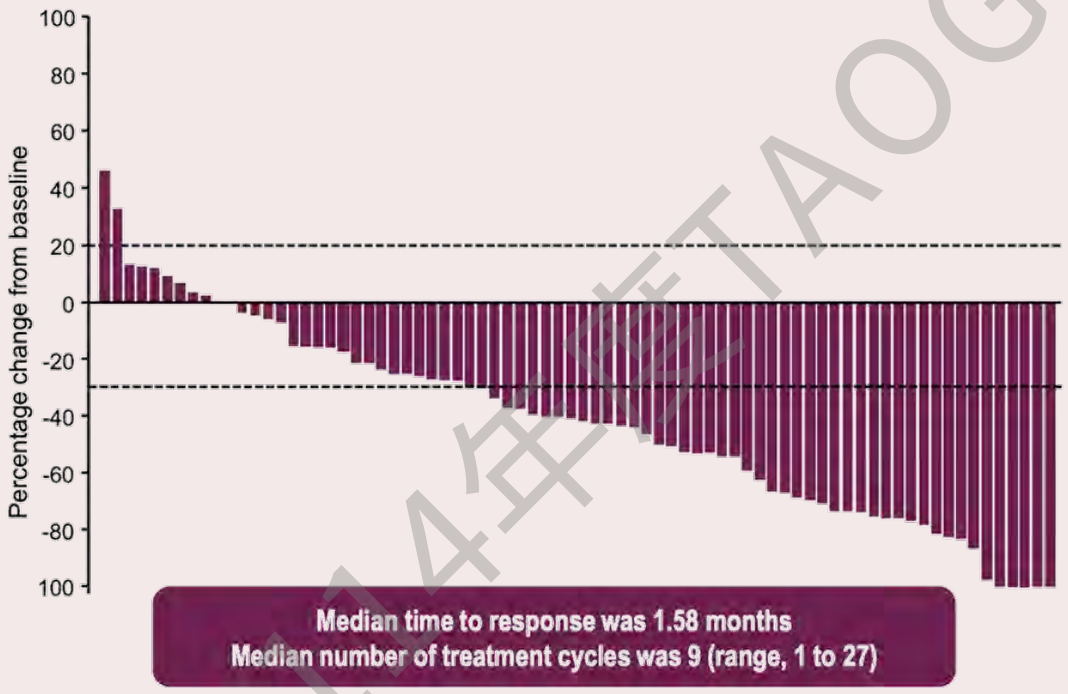
Antibody Drug Conjugates - MIRV

PICCOLO TRIAL

Investigator-Assessed Efficacy Measures

BARCELONA 2024 ESMO congress

Maximum Tumor Percentage Change From Baseline With MIRV



Data cutoff: January 17, 2024.

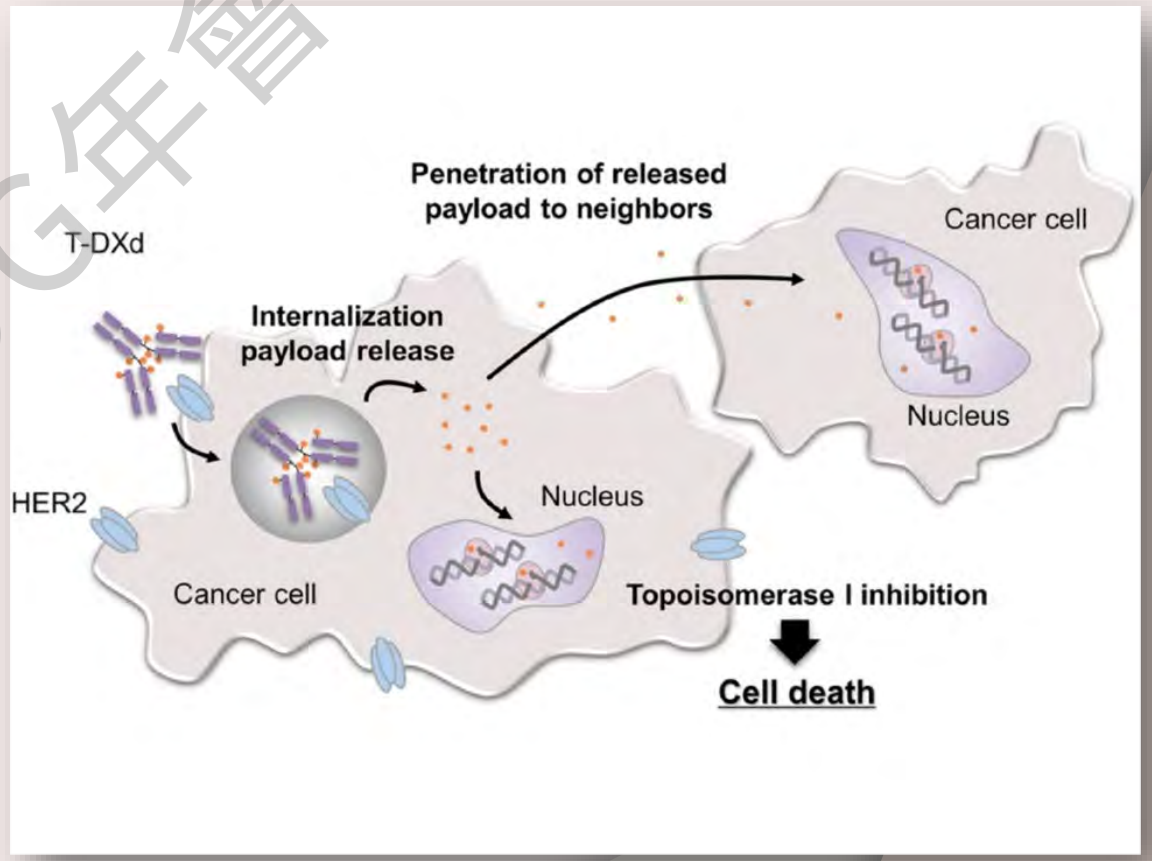
Primary Endpoint	N=79
ORR, n (%)	41 (51.9)
95% CI	40.4-63.3
Best overall response, n (%)	
CR	6 (7.6)
PR	35 (44.3)
SD	29 (36.7)
PD	7 (8.9)
Not evaluable	2 (2.5)

Secondary Endpoints	
Median DOR[a]	n=41
Months (95% CI)	8.25 (5.55-10.78)
Median PFS	N=79
Months (95% CI)	6.93 (5.85-9.59)
CA-125 response[b]	n=47
n (%)	35 (74.5)
95% CI	59.7-86.1

Mirvetuximab Soravtansine (MIRV) in Recurrent Platinum-Sensitive Ovarian Cancer (PSOC) with High Folate Receptor-Alpha (FRα) Expression: Results From the Phase II PICCOLO Trial (ESMO 2024)

Antibody Drug Conjugates – T-Dxd

- Trastuzumab deruxtecan (T-Dxd/EnHertu)
  - Humanized HER2 monoclonal IgG1 antibody
  - Topoisomerase I inhibitor
  - Drug-to-antibody ratio: 8:1



Antibody Drug Conjugates – T-Dxd

DESTINY - Pan tumor02

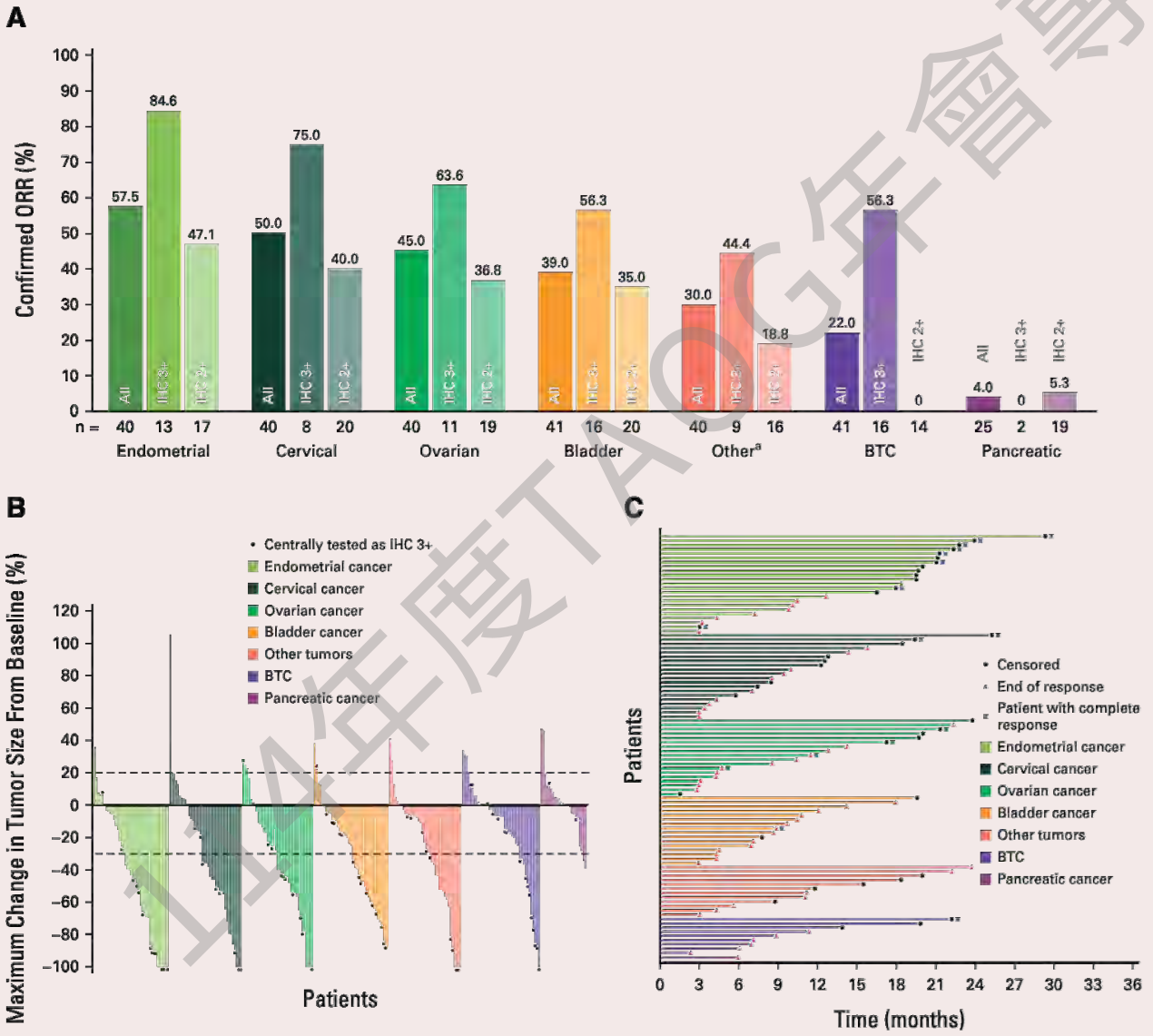
- ✓ **Open-label, Phase II**
- **Locally advanced or metastatic disease**
  - **After ≥1 systemic treatment**
  - **(or) Without alternative treatments**
- **HER2-expressing**
  - **Immunohistochemistry [IHC] 3+/2+**
  - **Local or central testing**
- ✓ **T-DXd (5.4 mg/kg) Q3W**
- ✓ **Response Rate (OvCA):**
- **HER2 3+: 63.6%; HER2 2+: 36.8%**

Baseline Characteristic	Endometrial Cancer (n = 40)	Cervical Cancer (n = 40)	Ovarian Cancer (n = 40)	Bladder Cancer (n = 41)	Other Tumors (n = 40)	Biliary Tract Cancer (n = 41)	Pancreatic Cancer (n = 25)
Age, years, median (range)	67 (37-79)	49 (28-78)	56 (34-72)	67 (43-85)	61 (38-81)	64 (31-80)	62 (23-80)
Female, No. (%)	40 (100.0)	40 (100.0)	40 (100.0)	14 (34.1)	13 (32.5)	21 (51.2)	10 (40.0)
Race, No. (%)							
White	23 (57.5)	29 (72.5)	22 (55.0)	25 (67.0)	27 (67.5)	20 (48.8)	17 (68.0)
Black or African American	4 (10.0)	0	1 (2.5)	0	0	0	1 (4.0)
Asian	10 (25.0)	7 (17.5)	17 (42.5)	16 (39.0)	10 (25.0)	21 (51.2)	6 (24.0)
Other	0	3 (7.5)	0	0	2 (5.0)	0	1 (4.0)
Not reported	3 (7.5)	1 (2.5)	0	0	1 (2.5)	0	0
ECOG performance status,[a] No. (%)							
0	23 (57.5)	22 (55.0)	26 (65.0)	19 (46.3)	15 (37.5)	13 (31.7)	8 (32.0)
1	17 (42.5)	18 (45.0)	13 (32.5)	22 (53.7)	25 (62.5)	28 (68.3)	17 (68.0)
2	0	0	1 (2.5)	0	0	0	0
HER2 testing for eligibility,[b] No. (%)							
Local	31 (77.5)	23 (57.5)	37 (92.5)	33 (80.5)	29 (72.5)	34 (82.9)	15 (60.0)
Central	9 (22.5)	17 (42.5)	3 (7.5)	8 (19.5)	11 (27.5)	7 (17.1)	10 (40.0)
HER2 IHC status (eligibility),[c] No. (%)							
IHC 3+	16 (40.0)	10 (25.0)	15 (37.5)	27 (65.9)	16 (40.0)	22 (53.7)	5 (20.0)
IHC 2+	24 (60.0)	25 (62.5)	25 (62.5)	14 (34.1)	24 (60.0)	19 (46.3)	20 (80.0)
IHC 1+[d]	0	5 (12.5)	0	0	0	0	0
Centrally confirmed HER2 IHC status, No. (%)							
IHC 3+	13 (32.5)	8 (20.0)	11 (27.5)	16 (39.0)	9 (22.5)	16 (39.0)	2 (8.0)
IHC 2+	17 (42.5)	20 (50.0)	19 (47.5)	20 (48.8)	16 (40.0)	14 (34.1)	19 (76.0)
IHC 1+	4 (10.0)	8 (20.0)	5 (12.5)	2 (4.9)	2 (5.0)	3 (7.3)	1 (4.0)
IHC 0	5 (12.5)	4 (10.0)	5 (12.5)	2 (4.9)	4 (10.0)	7 (17.1)	3 (12.0)
Unknown[e]	1 (2.5)	0	0	1 (2.4)	9 (22.5)	1 (2.4)	0
Prior therapy lines							
Median (range)	2 (0-7)	2 (1-6)	3 (1-12)	2 (0-9)	2 (0-8)	2 (1-5)	2 (1-4)
0, No. (%)	1 (2.5)	0	0	1 (2.4)	1 (2.5)	0	0
1, No. (%)	8 (20.0)	6 (15.0)	8 (20.0)	13 (31.7)	15 (37.5)	14 (34.1)	7 (28.0)
2, No. (%)	18 (45.0)	15 (37.5)	8 (20.0)	8 (19.5)	9 (22.5)	15 (36.6)	11 (44.0)
3, No. (%)	6 (15.0)	9 (22.5)	5 (12.5)	10 (24.4)	10 (25.0)	9 (22.0)	6 (24.0)
4, No. (%)	3 (7.5)	6 (15.0)	5 (12.5)	4 (9.8)	0	2 (4.9)	1 (4.0)
≥5, No. (%)	4 (10.0)	4 (10.0)	14 (35.0)	5 (12.2)	5 (12.5)	1 (2.4)	0
Prior HER2 therapy, No. (%)	9 (22.5)	1 (2.5)	2 (5.0)	3 (7.3)	14 (35.0)	7 (17.1)	2 (8.0)
Trastuzumab	5 (12.5)	1 (2.5)	2 (5.0)	3 (7.3)	14 (35.0)	6 (14.6)	2 (8.0)
Pertuzumab	0	1 (2.5)	0	1 (2.4)	2 (5.0)	1 (2.4)	0
Zanidatamab	2 (5.0)	0	0	0	1 (2.5)	1 (2.4)	0
Trastuzumab emtansine	1 (2.5)	1 (2.5)	0	1 (2.4)	0	0	0
Trastuzumab duocarmazine	1 (2.5)	0	0	0	0	0	0
Tucatinib	0	0	0	0	0	0	1 (4.0)

Meric-Bernstam F, et al. Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial. J Clin Oncol. 2024 Jan 1;42(1):47-58. doi: 10.1200/JCO.23.02005. Epub 2023 Oct 23. PMID: 37870536; PMCID: PMC10730032.

Antibody Drug Conjugates – T-Dxd

DESTINY PAN TUMOR-02



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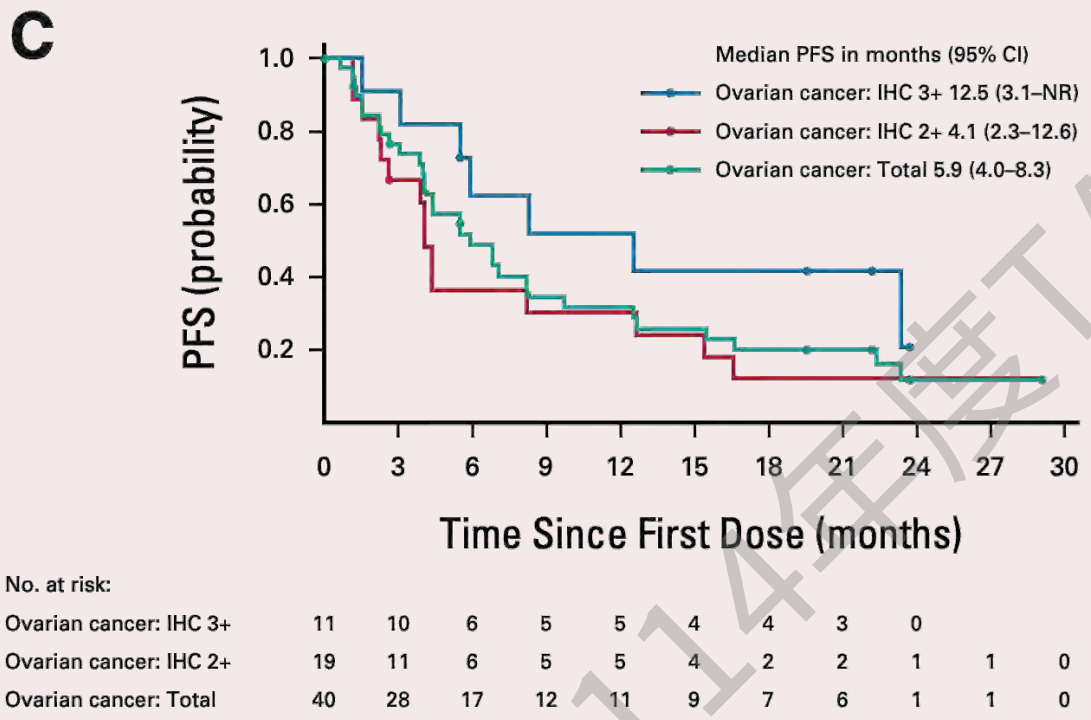
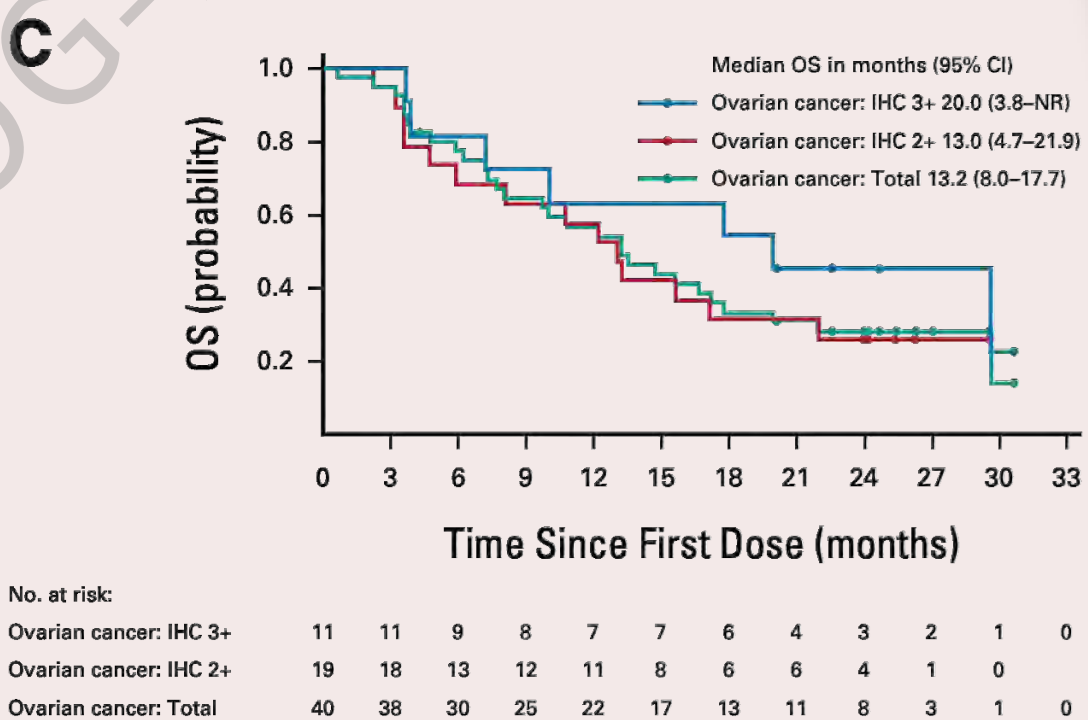
Antibody Drug Conjugates – T-Dxd

DESTINY PAN TUMOR-02



No. at risk:											
Ovarian cancer: IHC 3+	11	10	6	5	5	4	4	3	0		
Ovarian cancer: IHC 2+	19	11	6	5	5	4	2	2	1	1	0
Ovarian cancer: Total	40	28	17	12	11	9	7	6	1	1	0



No. at risk:												
Ovarian cancer: IHC 3+	11	11	9	8	7	7	6	4	3	2	1	0
Ovarian cancer: IHC 2+	19	18	13	12	11	8	6	6	4	1	0	
Ovarian cancer: Total	40	38	30	25	22	17	13	11	8	3	1	0

Meric-Bernstam F, et al. Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial. J Clin Oncol. 2024 Jan 1;42(1):47-58. doi: 10.1200/JCO.23.02005. Epub 2023 Oct 23. PMID: 37870536; PMCID: PMC10730032.

Antibody Drug Conjugates – T-Dxd

DESTINY PAN TUMOR-02

TABLE 2. Incidence of Drug-Related Adverse Events

Adverse Event	Endometrial Cancer (n = 40)	Cervical Cancer (n = 40)	Ovarian Cancer (n = 40)	Bladder Cancer (n = 41)	Other Tumors (n = 40)	Biliary Tract Cancer (n = 41)	Pancreatic Cancer (n = 25)
Drug-related adverse events, No. (%)	36 (90.0)	36 (90.0)	34 (85.0)	38 (92.7)	34 (85.0)	33 (80.5)	15 (60.0)
Grade ≥3	14 (35.0)	19 (47.5)	21 (52.5)	17 (41.5)	15 (37.5)	16 (39.0)	7 (28.0)
Serious adverse events	4 (10.0)	3 (7.5)	11 (27.5)	4 (9.8)	6 (15.0)	5 (12.2)	3 (12.0)
Leading to discontinuation	3 (7.5)	3 (7.5)	1 (2.5)	4 (9.8)	6 (15.0)	5 (12.2)	1 (4.0)
Leading to dose modification[a]	13 (32.5)	13 (32.5)	18 (45.0)	15 (36.6)	13 (32.5)	13 (31.7)	0
Associated with death	2 (5.0)	0	0	1 (2.4)	1 (2.5)	0	0
Most common drug-related adverse events (>10% of total patients), No. (%)							
Nausea	29 (72.5)	26 (65.0)	22 (55.0)	21 (51.2)	23 (57.5)	19 (46.3)	7 (28.0)
Anemia	7 (17.5)	15 (37.5)	15 (37.5)	12 (29.3)	11 (27.5)	10 (24.4)	4 (16.0)
Diarrhea	16 (40.0)	15 (37.5)	8 (20.0)	13 (31.7)	6 (15.0)	8 (19.5)	3 (12.0)
Fatigue	10 (25.0)	9 (22.5)	11 (27.5)	11 (26.8)	12 (30.0)	9 (22.0)	4 (16.0)
Vomiting	16 (40.0)	10 (25.0)	7 (17.5)	6 (14.6)	15 (37.5)	9 (22.0)	3 (12.0)
Neutropenia	4 (10.0)	8 (20.0)	5 (12.5)	11 (26.8)	9 (22.5)	9 (22.0)	4 (16.0)
Decreased appetite	8 (20.0)	7 (17.5)	8 (20.0)	8 (19.5)	7 (17.5)	7 (17.1)	2 (8.0)
Asthenia	11 (27.5)	9 (22.5)	6 (15.0)	3 (7.3)	8 (20.0)	6 (14.6)	3 (12.0)
Alopecia	9 (22.5)	8 (20.0)	5 (12.5)	5 (12.2)	7 (17.5)	9 (22.0)	2 (8.0)
Thrombocytopenia	2 (5.0)	2 (5.0)	5 (12.5)	6 (14.6)	7 (17.5)	5 (12.2)	3 (12.0)

[a]Dose modification includes adverse events with action taken of dose reduced or drug interrupted. Adverse events associated with death included pneumonia (n = 1), organizing pneumonia (n = 1), pneumonitis (n = 1), and neutropenic sepsis (n = 1).

ILD/pneumonitis occurred in 28 (10.5%) patients

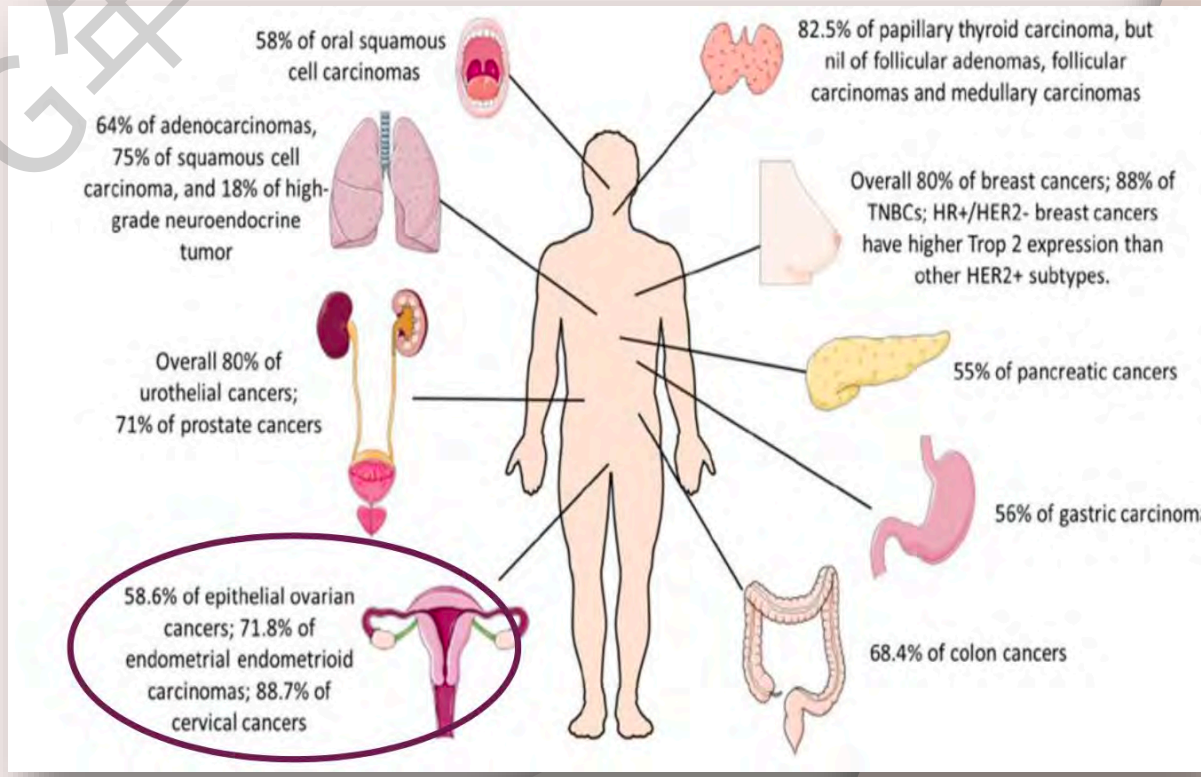
Low grade: (grade 1, n = 7 [2.6%]; grade 2, n = 17 [6.4%]). Grade 3: n = 1 [0.4%]

Three (1.1%) fatal adjudicated drug-related cases of ILD/pneumonitis

Meric-Bernstam F, et al. Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial. J Clin Oncol. 2024 Jan 1;42(1):47-58. doi: 10.1200/JCO.23.02005. Epub 2023 Oct 23. PMID: 37870536; PMCID: PMC10730032.

Antibody Drug Conjugates – TROP2

- Trophoblast cell surface antigen 2 (TROP2)
  - Transmembrane calcium signal transducer
  - Promoting tumor proliferation
    - ✓ Regulating the calcium ion signaling pathway
    - ✓ Cyclin expression and reducing fibronectin adhesion



Antibody Drug Conjugates – TROP2

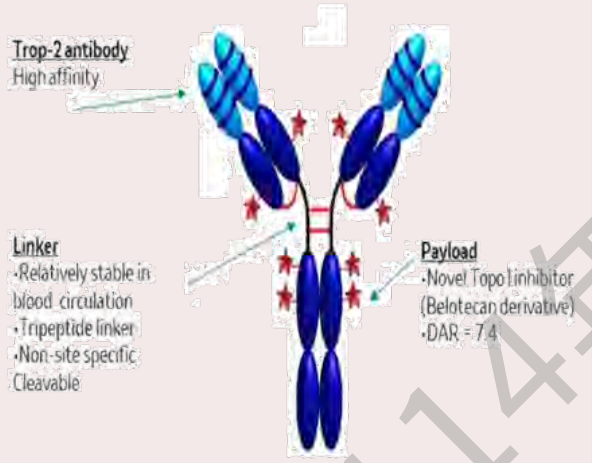
BARCELONA 2024 ESMO congress

Sacituzumab Tirumotecan (MK-2870)

Moving into a randomized phase III in the maintenance setting

ADC targeting TROP2

Sacituzumab tirumotecan



Efficacy

MK-2870-001 is the FIH, Phase 1/2 study evaluating MK-2870 in participants with locally advanced unresectable/metastatic solid tumors (including OC) who are refractory to available standard therapies.

Participants with **OC (n=40)**, who had received at least 1 prior line of platinum based therapy and were deemed **platinum-resistant**, were enrolled and treated with MK-2870 5 mg/kg q2w in the study.

The **ORR** (confirmed + unconfirmed) based on investigator assessment per RECIST 1.1 for these participants was **40.0%** (95% CI: 24.9, 56.7).

Safety

	All Grade	≥Grade 3
TRAEs	41 (95.3)	29 (67.4)
TRAEs associated with dose delay	21 (48.8)	17 (39.5)
TRAEs associated with dose reduction	10 (23.3)	9 (20.9)
TRAEs associated with discontinuation	0	0
Treatment-related SAEs	9 (20.9)	9 (20.9)
TRAEs associated with death	0	0
TRAEs by preferred term in ≥20% of patients		
Anemia	31 (72.1)	13 (30.2)
White blood cell count decreased	24 (55.8)	10 (23.3)
Alopecia	23 (53.5)	0
Neutrophil count decreased	23 (53.5)	14 (32.6)
Stomatitis	21 (48.8)	4 (9.3)
Rash	17 (39.5)	3 (7.0)
Nausea	16 (37.2)	0
Decreased appetite	15 (34.9)	0
Vomiting	14 (32.6)	2 (4.7)
Platelet count decreased	10 (23.3)	1 (2.3)
Hypoalbuminemia	9 (20.9)	0

Antibody Drug Conjugates – TROP2

Datopotomab deruxtecan (Dato-DXd)

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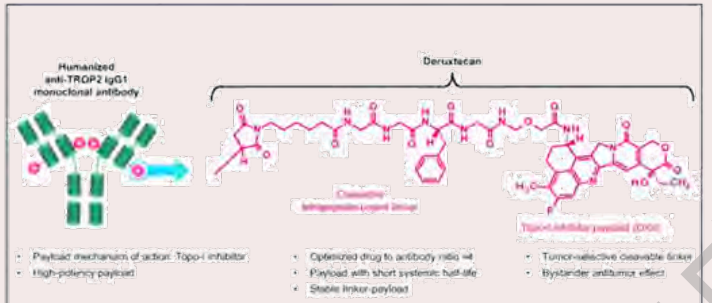
Anti-TROP2 monoclonal antibody

Dato-DXd



- Humanized anti-TROP2 IgG1 monoclonal antibody
- Tetrapeptide-based cleavable linker
- Payload: Topoisomerase I inhibitor

TROPION-Pan Tumor03 (NCT05489211)

An ongoing phase 2, open-label, study

The promising activity demonstrated in early-phase trials (e.g. TROPION-PanTumor01, TROPION-Lung02, and BEGONIA), provides a rationale for investigating Dato-DXd as monotherapy and combination therapy across different types of solid tumor

Antibody Drug Conjugates – TROP2

Efficacy in Ovarian Cancer

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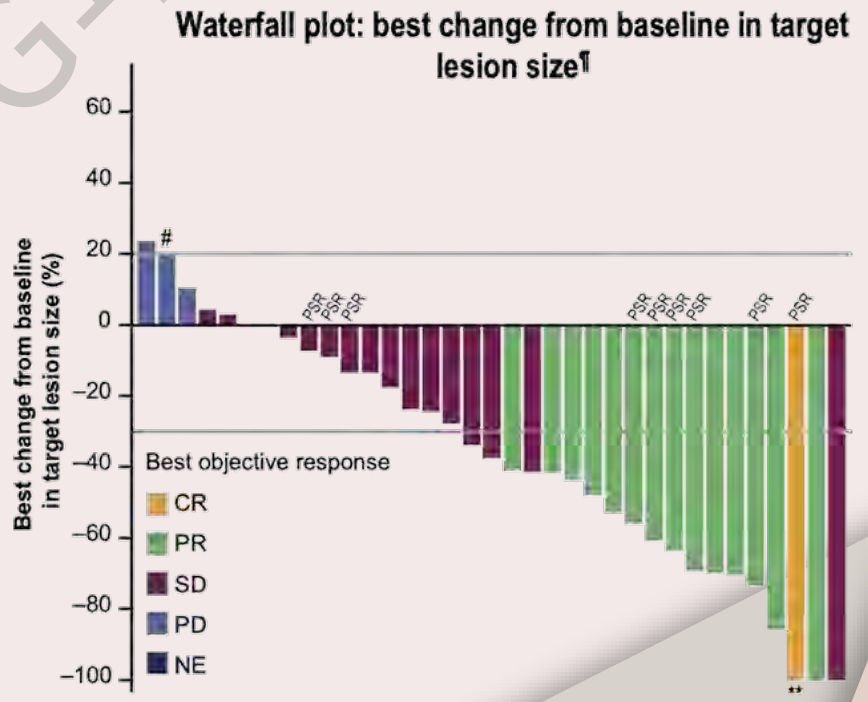
- As of June 14, 2024, median duration of follow-up* was 14.5 months (range 10.4–15.4) in the ovarian cohort

	Ovarian		
	Total (N=35)	Platinum-sensitive (n=9)	Platinum-resistant (n=26)
Confirmed ORR, % (95% CI)	42.9 (26.3–60.6)	66.7 (29.9–92.5)	34.6 (17.2–55.7)
Best overall response, n (%)			
CR	1 (2.9)	1 (11.1)	0 (0.0)
PR	14 (40.0)	5 (55.6)	9 (34.6)
SD†	17 (48.6)	3 (33.3)	14 (53.8)
PD‡	3 (8.6)	0 (0.0)	3 (11.5)
NE§	0 (0.0)	0 (0.0)	0 (0.0)
Median time to response, months (range)	1.4 (1.2–8.2)	–	–
Median DoR, months (95% CI)	5.7 (2.9–NC)	8.5 (2.7–NC)	5.6 (2.9–NC)
DCR at 12 weeks,‖ % (80% CI)	85.7 (75.1–92.9)	100 (77.4–100.0)	80.8 (67.2–90.3)
Median PFS, months (95% CI)	5.6 (4.1–7.0)	–	–



*Duration of follow-up calculated as the median time from randomisation to the date of censoring, in censored patients only; †Unconfirmed CR/PR, or SD ≥35 days; ‡RECIST progression or death ≤13 weeks; §SD <35 days, no valid baseline assessment or evaluable follow-up assessment; ‖Defined as the percentage of patients who achieved CR, PR or SD; ¶Best change in target lesion size is the maximum reduction from baseline or the minimum increase from baseline in the absence of a reduction. Lines at -30% and 20% indicate thresholds for PR and PD, respectively. If best percentage change cannot be calculated due to missing data, +20% will be imputed as the best percentage change in the following situations (otherwise left as missing): patient has no post-baseline assessment, has died, has new lesions or progression of lesions, or has withdrawn due to PD and has no evaluable target lesion data. Patients with imputed values marked with #; **Patient had PR at the first visit (with a change from baseline in the target lesion of 100%) and PD at the subsequent two visits and was therefore an unconfirmed PR and classified as SD. CI, confidence interval; CR, complete response; NC, not calculable; NE, not evaluable; PD, progressive disease; PR, partial response; PSR, platinum-sensitive relapsed; SD, stable disease.

The development of ADCs for Ovarian cancer

Target Antigen (Expression% in OC)	Agent Name	Anti-Body Type	Linker Name (Type)	Paylord Name (Target)	Common TRAEs	Development Status for OC	Development of Combination Therapy
FRα (50–80%)	MIRV	IgG1-kappa	N-Succinimidyl 4-(2 pyridyldithio)-2-sulfobutanoate linker (Cleavable)	DM4 (tubulin)	ocular events, diarrhea, fatigue, nausea, vomiting, peripheral, neuropathy, netropenia	FDA approved	O
	MORAb-202	IgG1-kappa	A reduced interchain disulfide bonds to maleimido-PEG2-valine-citrulline-p-aminobenzylcarbamyl linker (Cleavable)	Eribulin (tubulin)	ILD/pneumonitis, nausea, pyrexia, malaise, headache	ongoing Phase II	
	STRO-002 (luvelta)	IgG1	valine citrulline p-aminobenzyl carbamate linker (Cleavable)	SC209 (tubulin)	neutropenia, arthralgia, anemia, neutropenia	ongoing Phase II	
TROP2 (50–60%)	Dato-DXd	IgG1	A tetrapeptide-based linker (Cleavable)	Deruxtecan (topoiso-merase I)	nausea, anemia, decreased WBC, ILD/pneumonitis,	ongoing Phase II	O
	ESG401	IgG1	unrevealed linker	SN38 (topoiso-merase I)	leukopenia, neutropenia, anemia, fatigue, nausea, vomiting, thrombocytop-enia, diarrhea, skin rash, oral mucositis	ongoing Phase II	
	IMMU-132 (SG)	IgG1-kappa	hRS7 via a hydrolysable CL2A linker (cleavable)	Govitecan (topoiso-merase I)	neutropenia, decreased WBC, anaemia, diarrhoea, fatigue, febrile, neutropenia, hypophos-phatemia, diarrhoea	ongoing Phase II	
HER2 (12–30%)	T-DXd	IgG1-kappa	Gly-Phe-Leu-Gly (tetrapeptide)	Deruxtecan (topoiso-merase I)	nausea, anemia, diarrhea, vomiting, fatigue, neutropenia, ILD/pneumonitis	possibility FDA approved *	
	SHR-A1811 (Trastumab rezetecan)	IgG1-kappa	unrevealed (cleavable)	SHR9265 (topoiso-merase I)	neutropenia, anemia, decreased WBC, ILD/pneumonitis	ongoing Phase II	
	RC48 (Disitamab vedotin)	IgG1-kappa	mc-val-cit-PABC (cleavable)	MMAE (tubulin)	peripheral sensory neuropathy, leukopenia, neutropenia, AST/ALT increased, alopecia, asthenia, decreased appetite	ongoing Phase II	
NaPi2b (66%)	UpRi	IgG1-kappa	Fleximer polymer scaffold (cleavable)	AF-HPA (tubulin)	AST increased, fatigue, anemia, thrombocytop-enia, neutropenia, peripheral neuropathy, ocular toxicity, ILD/pneumonitis	ongoing Phase III	
CDH6 (85%)	DS-6000 (R-Dxd)	IgG1	Tetrapeptide based linker (cleavable)	Deruxtecan (topoiso-merase I)	nausea, fatigue, vomiting, diarrhoea **	ongoing Phase II/III	

Sato S, Shoji T, Jo A, Otsuka H, Abe M, Tatsuki S, Chiba Y, Takatori E, Kaido Y, Nagasawa T, Kagabu M, Baba T. Antibody-Drug Conjugates: The New Treatment Approaches for Ovarian Cancer. Cancers (Basel). 2024 Jul 15;16(14):2545. doi: 10.3390/cancers16142545. PMID: 39061184; PMCID: PMC11275051.

Major Clinical Trial in 2024

Clinical Research in Ovarian cancer

Table 3. List of the major clinical research in ovarian cancer in 2024

Study name	Design	No.	Inclusion criteria	Intervention	Control	Primary endpoint	PFS	OS
First-line treatment, combination of immune checkpoint inhibitor and PARP inhibitor								
DUO-O	Phase III, randomized, double-blind	1,130	· Stage III–IV high-grade epithelial · No prior systemic therapy · Non-tBRCAm	TC + bevacizumab + durvalumab, followed by maintenance bevacizumab + durvalumab + olaparib	TC + bevacizumab + placebo, followed by maintenance bevacizumab + placebo + placebo	PFS by investigator	Median PFS: 25.1 vs. 19.3 mo, HR=0.61; 95% CI=0.51–0.73 HRD+ group, Median PFS: 45.1 vs. 23.3 mo, HR=0.46; 95% CI=0.33–0.65	HR=0.95; 95% CI=0.76–1.20; p=0.68 HRD+ group, HR=0.84; 95% CI=0.51–1.37
ATHENA combo	Phase III, randomized, double-blind	863	· Stage III–IV high-grade epithelial · Complete or partial response after first-line platinum-based chemotherapy	Maintenance rucaparib + nivolumab	Maintenance rucaparib + placebo	PFS by investigator	Median PFS: 15.0 vs. 20.2 mo, HR=1.29; 95% CI=1.08–1.53	Median OS: 49.4 vs. 58.0 mo, HR=1.13; 95% CI=0.93–1.38
First-line treatment, PARP inhibitor maintenance								
PRIMA	Phase III, randomized, double-blind	733	· Stage III with visible residual tumor after primary debulking surgery or inoperable stage III or IV · High-grade serous or endometrioid · Complete or partial response after first-line platinum-based chemotherapy	Maintenance niraparib	Maintenance placebo	PFS by BICR	5-yr PFS rate, 22% vs. 12%; HRD+ group, 35% vs. 16%; HRD− group, 8% vs. 7%	5-yr OS rate: 42% vs. 44%, HR=1.01; 95% CI=0.84–1.23; p=0.8834 HRD+ group: 55% vs. 56%, HR=0.95; 95% CI=0.70–1.29 HRD− group: 29% vs. 27%, HR=0.93; 95% CI=0.69–1.26
NeoPembrOV	Phase II, randomized, open label	91	· Stage IIIC/IV high-grade serous or endometrioid types · Upfront complete resection was unachievable · PCI score <30	TC + pembrolizumab, followed by maintenance pembrolizumab	TC	CRR at IDS	Median PFS, 19.4 vs. 20.8 mo; CRR, 74% vs. 70%; ORR, 72% vs. 60%	Median OS, 49.8 vs. 35.3 mo

(continued to the next page)

Lee SJ, Yoo JG, Kim JH, Park JY, Lee JY, Lee YY, Suh DH. Gynecologic oncology in 2024: breakthrough trials and evolving treatment strategies for cervical, uterine corpus, and ovarian cancers. J Gynecol Oncol. 2025 Jan;36(1):e72. https://doi.org/10.3802/jgo.2025.36.e72

Table 3. (Continued) List of the major clinical research in ovarian cancer in 2024

Study name	Design	No.	Inclusion criteria	Intervention	Control	Primary endpoint	PFS	OS
Platinum-sensitive recurrence								
ANITA	Phase III, randomized, double-blind	417	· Recurrent high-grade serous, endometrioid or undifferentiated · TFI >6 mo · ≤2 prior lines of chemotherapy	Carboplatin doublet + atezolizumab followed by maintenance atezolizumab + niraparib	Carboplatin doublet + placebo followed by maintenance placebo + niraparib	PFS by investigator	Median PFS: 11.2 vs. 10.1 mo, HR=0.92; 95% CI=0.74–1.13; p=0.28	Not available
ATALANTE	Phase III, randomized, double-blind	614	· Recurrent epithelial non-mucinous · TFI >6 mo · 1 or 2 prior chemotherapy lines	Carboplatin-based chemotherapy + bevacizumab + atezolizumab followed by maintenance atezolizumab	Carboplatin-based chemotherapy + bevacizumab + placebo followed by maintenance placebo	PFS	Median PFS: 13.6 vs. 11.3 mo, HR=0.83; 95% CI=0.69–0.98; p=0.035	Median OS, 35.75 vs. 30.62 mo
Platinum-resistant recurrence								
NRG-GY005	Phase II/III, randomised, open-label, superiority	562	· Platinum-refractory or resistant high-grade serous/ endometrioid · Evaluable disease	ARM 1: cediranib + olaparib ARM 2: cediranib	Weekly paclitaxel, topotecan or PLD	PFS, OS	Median PFS, ARM 1 vs. ARM 3: 5.2 vs. 3.4 mo, HR=0.796; 95% CI=0.597–1.060; p=0.145	Median OS, ARM 1 vs. ARM 3: 12.8 vs. 13.6 mo, HR=1.027; 95% CI=0.771–1.368
AGO-OVAR 2.29/ENGOT-ov34	Phase III, randomized, double-blind	574	· Recurrent high-grade serous, endometrioid or undifferentiated · 1st or 2nd relapse: Treatment-free interval <6 mo, or 3rd relapse	Weekly paclitaxel or PLD + bevacizumab + atezolizumab	Weekly paclitaxel or PLD + bevacizumab + placebo	PFS, OS	Median PFS: 6.3 vs. 6.6 mo, HR=0.88; 95% CI=0.73–1.05; p=0.15	Median OS: 14.3 vs 13.0 mo, HR=0.83; 95% CI=0.68–1.01; p=0.06
Clear cell carcinoma								
LARA	Phase II, open-label, two-stage	27	· Recurrent clear cell carcinoma of ovary or endometrium · Relapse after at least 1 line of platinum-based chemotherapy · Measurable disease	Pembrolizumab + lenvatinib	None	ORR at 24 wk	PFS at 12 wk, 60% (38.4–76.1); PFS at 24 wk, 48% (27.8–65.6); ORR at 24 wk, 44.0% (24.4–65.1)	NA
BrUOG 354	Phase II, randomized, Two-arm, two-stage	44	· Recurrent extra-renal clear cell carcinoma · Relapse after at least 1 line of platinum-based chemotherapy · Measurable disease	Arm 1: Nivolumab, Arm 2: Nivolumab + ipilimumab	None	ORR	Median PFS: ARM, 1: 2.2 mo; ARM, 2: 5.6 mo ORR: Arm 1, 14.3%; Arm 2, 33%	Median OS: Arm 1, 17 mo; Arm 2, 24.6 mo
Surgery								
SOC-1	Phase II/III, randomised, open-label	357	· Platinum-sensitive recurrence · Had one previous platinum-based chemotherapy, TFI >6 mo · Resectable disease according to the iMODEL and PET/CT	Secondary cytoreduction	No surgery	OS, PFS	Median PFS: 18.0 vs. 11.9 mo, HR=0.55; 95% CI=0.44–0.69; p<0.0001	Median OS: 58.1 vs. 52.1 mo, HR=0.80; 95% CI=0.61–1.05; p=0.11
CARACO	Phase III, randomised, open-label	379	· Newly diagnosed stage III–IV · No pre-and intra-operative suspicious lymph nodes >2 cm · Feasible optimal primary surgery or if not feasible interval surgery after NAC (residual tumor <1 cm)	No retroperitoneal pelvic and paraaortic lymphadenectomy	Retroperitoneal pelvic and paraaortic lymphadenectomy	PFS	Median PFS: 14.8 vs. 18.5 mo, HR=0.98; 95% CI=0.78–1.22; p=0.86	Median OS: 48.9 vs. 58.0 mo, HR=0.96; 95% CI=0.75–1.22; p=0.72

Take Home Message

- Maintenance therapy has evolved significantly for ovarian cancer, with two major classes of drugs showing efficacy: anti-angiogenic agents and PARP inhibitors.
- The effectiveness of maintenance therapy depends on patient stratification - particularly BRCA mutation status and homologous recombination deficiency (HRD) status for PARP inhibitors.
- For platinum-resistant recurrent ovarian cancer, antibody-drug conjugates (ADCs) show promising results
- Combination strategies are emerging as effective approaches, particularly for difficult-to-treat platinum-resistant disease.
- Novel targets of ADCs are being explored in clinical trials with encouraging early results, expanding treatment options beyond traditional therapies.

Thank for Your Attention