

The frontline chemotherapy for patients with epithelial ovarian cancer: Focusing FLORA-05 study and Taiwan experience

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EAGOT

03, September, 2023

A modified form from original Dr. Szu-Ting Yang's slides



I do not have any conflict for this talk

Outline

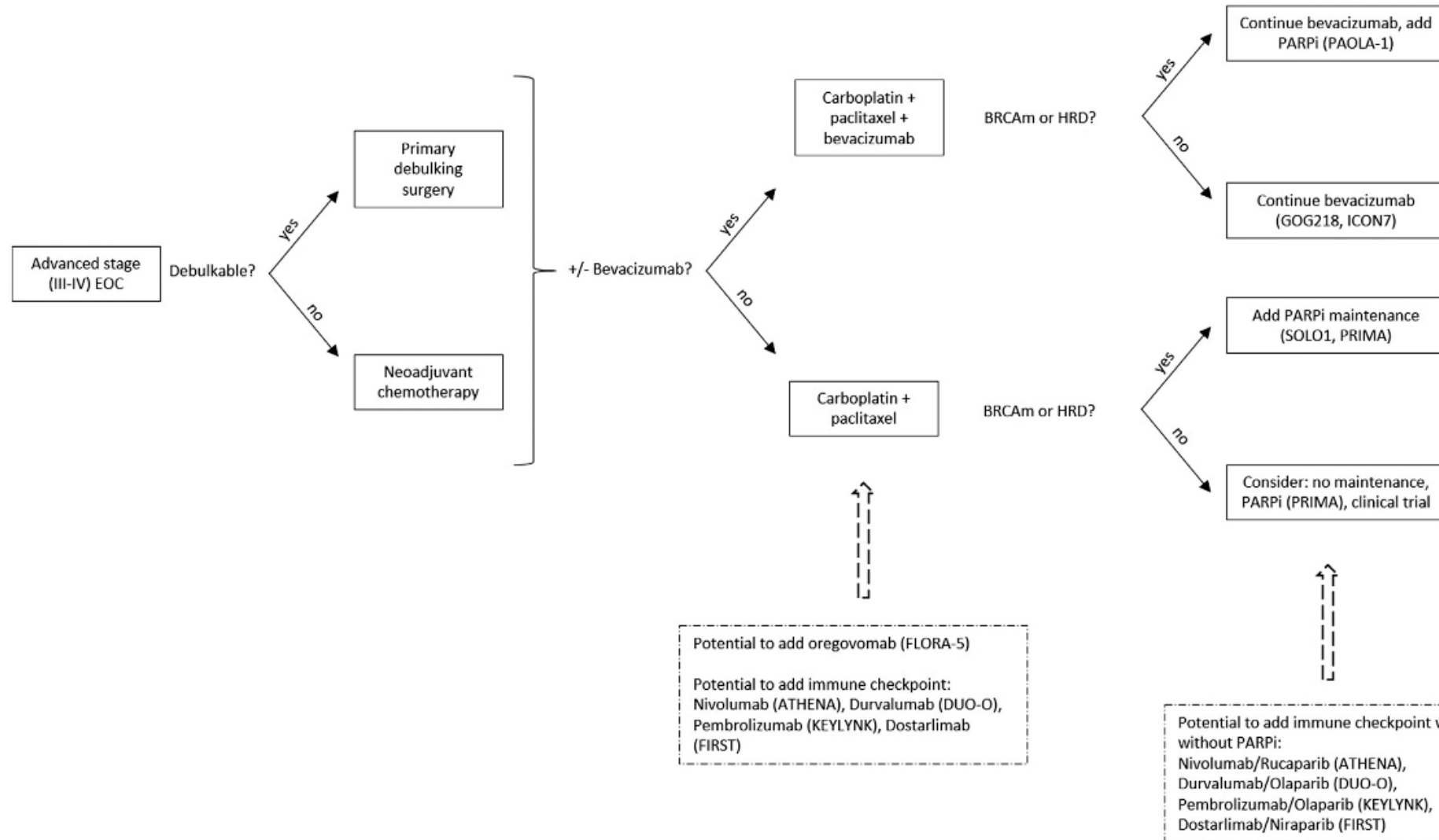
- ◆ **The frontline therapy of epithelial ovarian cancer (EOC)**
- ◆ The perspective of Taiwan gynecologic oncologists
- ◆ Oregovomab background
- ◆ Oregovomab development status
- ◆ FLORA-05 study and FLORA-06 study
- ◆ Take Home Message

Primary treatment modality for EOC

Primary treatment modality

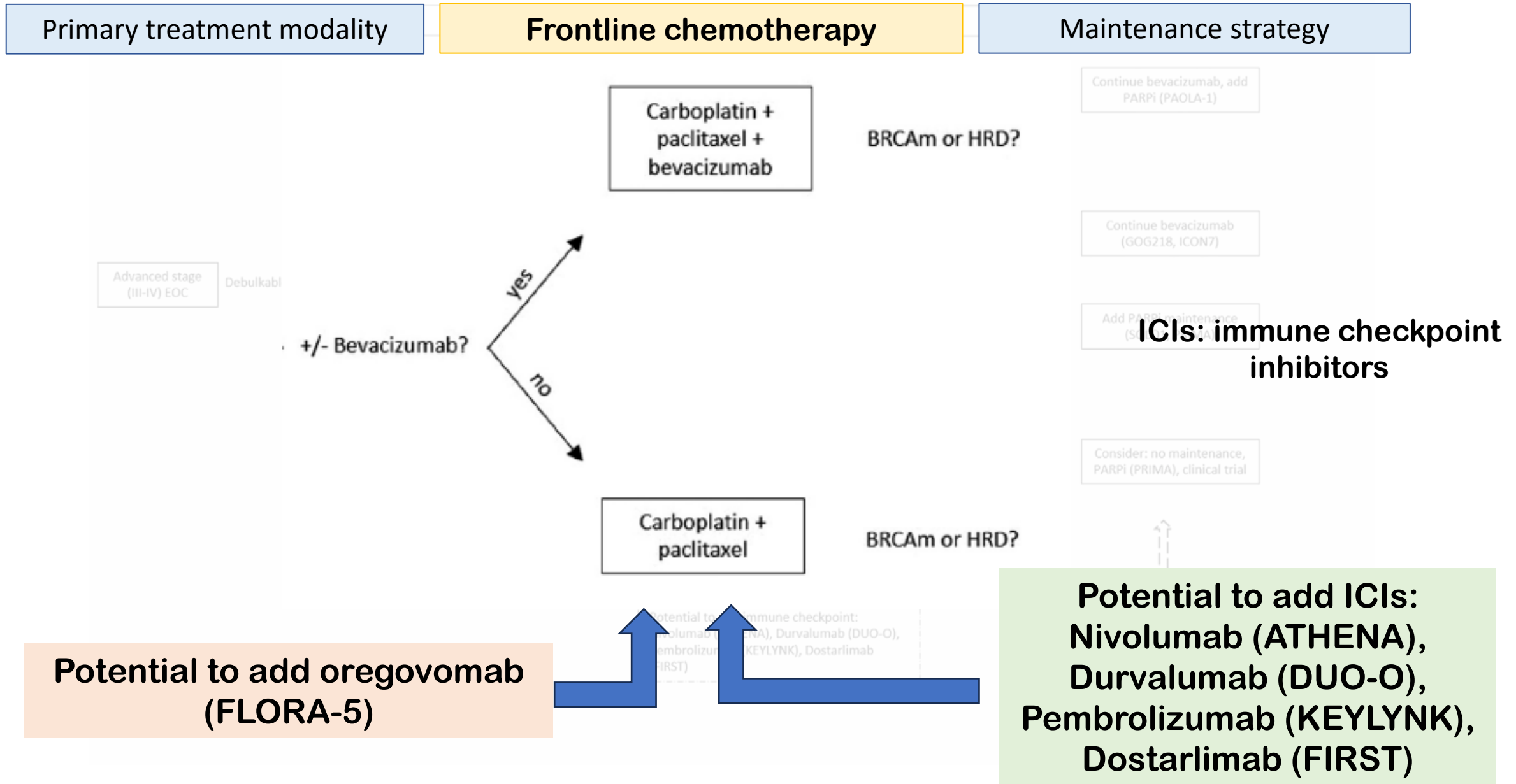
Frontline chemotherapy

Maintenance strategy

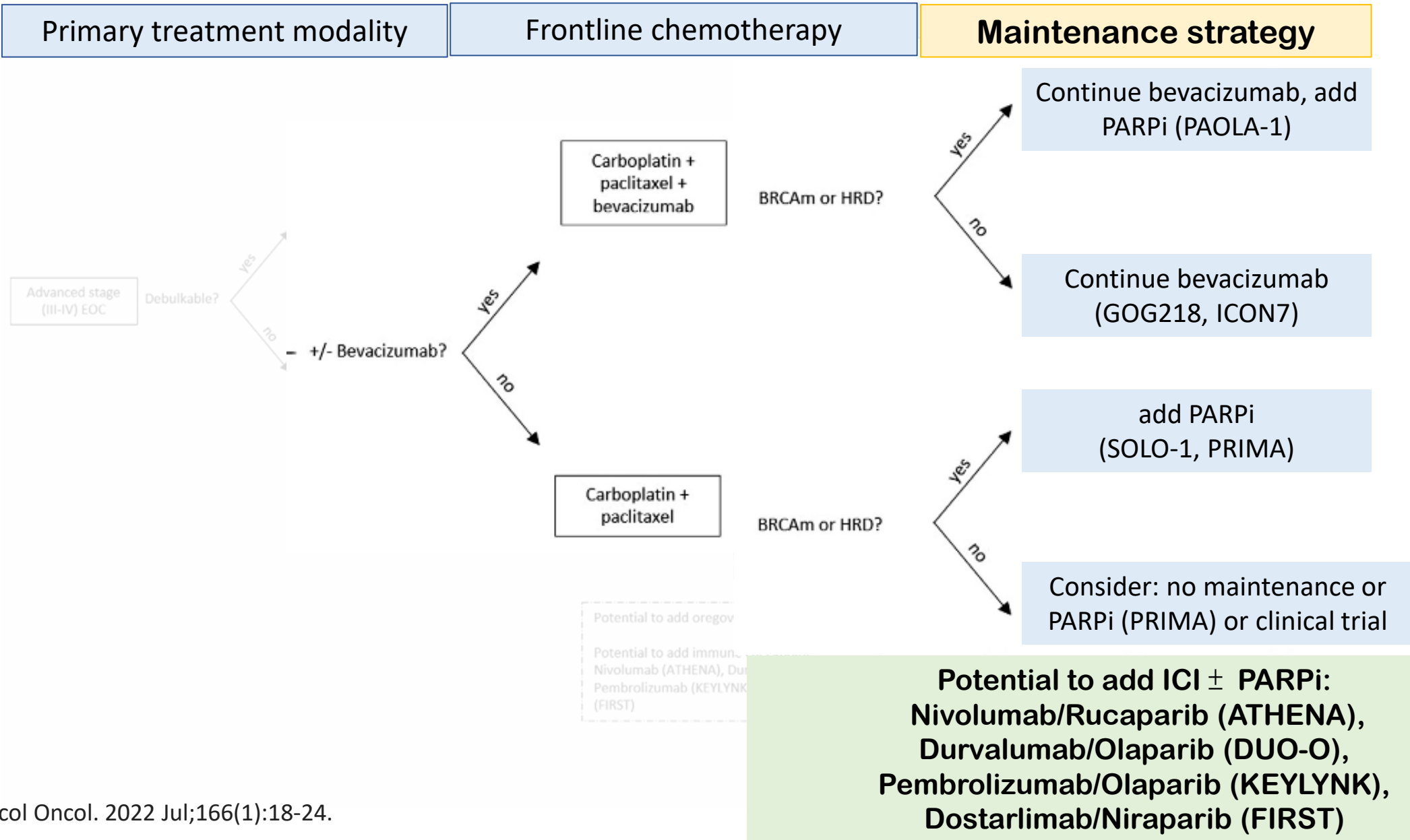


The frontline therapy of EOC

Gynecol Oncol. 2022 Jul;166(1):18-24.



Maintenance strategy for EOC



Outline

- ◆ Frontline therapy of epithelial ovarian cancer (EOC)
- ◆ The perspective of Taiwan gynecologic oncologists
- ◆ Oregovomab background
- ◆ Oregovomab development status
- ◆ FLORA-05 study and FLORA-06 study
- ◆ Take Home Message

The perspective of Taiwan gynecologic oncologists

- Aim: Pattern of practice for frontline therapy of EOC in Taiwan
- A questionnaire paper-based survey
- At the 2023 seasonal conference of Taiwan Association of Gynecologic Oncologists on 19 August 2023.
- Response rate 39/109=35.8%

		Number (%)
Types of medical facilities	Medical Center	31 (79.5)
	Regional Hospital	6 (15.4)
	Municipal Hospital	2 (5.1)
Age of physician	≤40	10 (25.6)
	41~50	7 (17.9)
	51~60	16 (41.0)
	≥61	6 (15.5)

The regimen of chemotherapy

	Stage I	Number (%)	Stage II to IV	Number (%)
mucinous	None	3 (7.9)	None	0 (0)
	Paclitaxel/carboplatin	29 (76.3)	Paclitaxel/carboplatin	30 (76.9)
	Paclitaxel/cisplatin	1 (2.6)	Paclitaxel/cisplatin	1 (2.6)
	5-FU/leucovorin/oxaliplatin	3 (7.9)	5-FU/leucovorin/oxaliplatin	5 (12.8)
	Capecitabine/oxaliplatin	2 (5.3)	Capecitabine/oxaliplatin	1 (2.6)
			Paclitaxel/carboplatin or 5-FU/leucovorin/oxaliplatin	2 (5.1)
low-grade serous	None	13 (35.1)	None	1 (2.6)
	Paclitaxel/carboplatin	23 (62.2)	Paclitaxel/carboplatin	36 (94.7)
	Paclitaxel/cisplatin	1 (2.7)	Paclitaxel/cisplatin	1 (2.6)
low-grade endometrioid	None	12 (32.4)	None	1 (2.6)
	Paclitaxel/carboplatin	25 (67.6)	Paclitaxel/carboplatin	37 (94.9)
	Paclitaxel/cisplatin	0 (0)	Paclitaxel/cisplatin	1 (2.6)

	Stage I	Number (%)	Stage II to IV	Number (%)
high-grade serous	None	1 (2.6)	None	0 (0)
	Paclitaxel/carboplatin	37 (94.9)	Paclitaxel/carboplatin	38 (97.4)
	Paclitaxel/cisplatin	1 (2.6)	Paclitaxel/cisplatin	1 (2.6)
high-grade endometrioid	None	1 (2.6)	None	0 (0)
	Paclitaxel/carboplatin	37 (94.9)	Paclitaxel/carboplatin	39 (100)
	Paclitaxel/cisplatin	1 (2.6)	Paclitaxel/cisplatin	0 (0)
clear cell carcinoma	None	0 (0)	None	0 (0)
	Paclitaxel/carboplatin	39 (100)	Paclitaxel/carboplatin	39 (100)
	Paclitaxel/cisplatin	0 (0)	Paclitaxel/cisplatin	0 (0)
carcinosarcoma	None	0 (0)	None	0 (0)
	Paclitaxel/carboplatin	33 (84.6)	Paclitaxel/carboplatin	36 (92.3)
	Paclitaxel/cisplatin	2 (5.1)	Paclitaxel/cisplatin	0 (0)
	Carboplatin/ifosfamide	0 (0)	Carboplatin/ifosfamide	1 (2.6)
	Cisplatin/ifosfamide	2 (5.1)	Cisplatin/ifosfamide	2 (5.1)
	Paclitaxel/ifosfamide	0 (0)	Paclitaxel/ifosfamide	0 (0)
	Paclitaxel/carboplatin or Carboplatin/ifosfamide or Cisplatin/ifosfamide	1 (2.6)		
	Paclitaxel/carboplatin or Paclitaxel/ifosfamide	1 (2.6)		

Dose-dense chemotherapy

Consider dose-dense chemotherapy?	Number (%)
No	18 (46.2)
Yes	21 (53.8)

- Dose-dense chemotherapy outcome in our hospital (PFS 36.5m/o, OS 56.0m/o) is not inferior to the standard therapy plus bevacizumab treatment, and the Japanese trial.
- Dose-dense weekly paclitaxel and triweekly cisplatin or triweekly carboplatin are both effective and feasible.



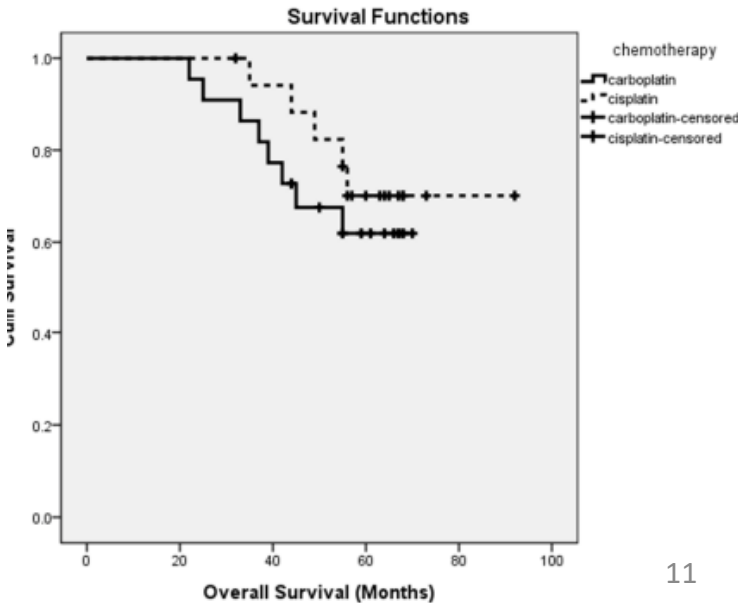
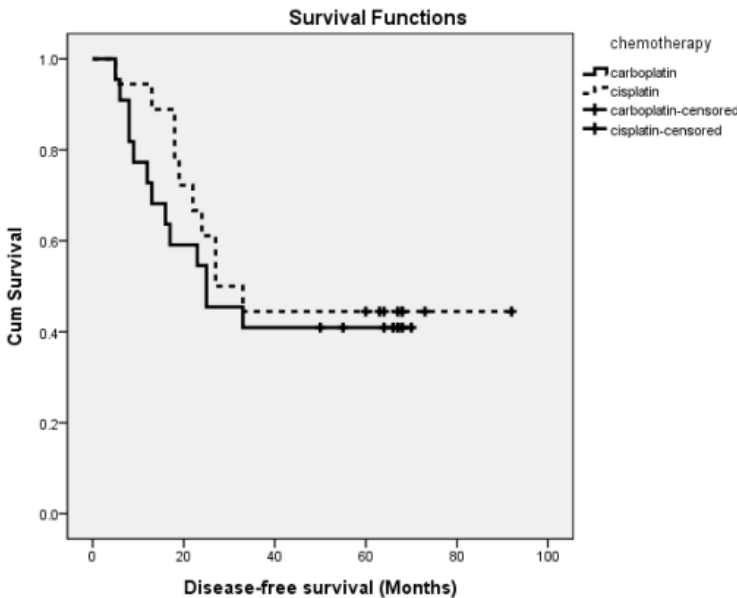
Article
Weekly Dose-Dense Paclitaxel and Triweekly Low-Dose Cisplatin: A Well-Tolerated and Effective Chemotherapeutic Regimen for First-Line Treatment of Advanced Ovarian, Fallopian Tube, and Primary Peritoneal Cancer

Min Cheng ^{1,2}, Howard Hao Lee ^{1,2}, Wen-Hsun Chang ^{1,3}, Na-Rong Lee ^{1,3}, Hsin-Yi Huang ⁴, Yi-Jen Chen ^{1,2,5}, Huann-Cheng Horng ^{1,2}, Wen-Ling Lee ^{6,7,*} and Peng-Hui Wang ^{1,2,5,8,9,*}



Article
Comparing Paclitaxel–Carboplatin with Paclitaxel–Cisplatin as the Front-Line Chemotherapy for Patients with FIGO IIIC Serous-Type Tubo-Ovarian Cancer

Chen-Yu Huang ^{1,2,3}, Min Cheng ^{1,2,3}, Na-Rong Lee ^{1,4}, Hsin-Yi Huang ⁵, Wen-Ling Lee ^{3,6,7}, Wen-Hsun Chang ^{1,3,4,*} and Peng-Hui Wang ^{1,2,3,8,9,*}



Considering to add bevacizumab in frontline

Adding bevacizumab	Stage I n (%)	Stage II n (%)	Stage III to IV n (%)
mucinous	0 (0)	7 (17.9)	32 (82.1)
high-grade serous	8 (20.5)	20 (51.3)	39 (100)
low-grade serous	0 (0)	10 (25.6)	30 (76.9)
low-grade endometrioid	1 (2.6)	9 (23.1)	32 (82.1)
high-grade endometrioid	6 (15.4)	17 (43.6)	39 (100)
clear cell carcinoma	12 (30.8)	25 (64.1)	39 (100)
carcinosarcoma	6 (15.4)	20 (51.3)	37 (94.9)

Considering NACT strategy

Condition:	Number (%)
Tumor invasion noted under colonoscopy (already excluding colon cancer)	23 (59.0)
Unclear margin of tumor and internal organs under CT or MRI	30 (76.9)
Never considering of NACT	0 (0)



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Journal of Gynecology Obstetrics
and Human Reproduction

journal homepage: www.elsevier.com

Original Article

Surgical management of patients with advanced ovarian cancer: Results of a French National Survey

Pierre-Alexis Gauci^{a,*}, Elise Deluche^b, Henri Azais^c, Francois Zaccarini^d, Benedetta Guani^e, Vincent Balaya^e, Yohan Kerbage^f, Floriane Jochum^g, Claire Sanson^d, Frédéric Guyon^h, Cherif Akladiosⁱ, Sofiane Bendifallah^j, Yohann Dabi^j

Criteria for deciding between primary surgery or neoadjuvant chemotherapy

Carcinosis score threshold	16 (40%)
Set of procedures to be performed to obtain complete resection	38 (95%)
Age of patient	30 (75%)
Visual appearance	9 (22.5%)
Personal beliefs about the best strategy	3 (7.5%)

NACT regimen and cycles

NACT regimen	Number (%)
Paclitaxel/carboplatin	23 (59.0)
Paclitaxel/cisplatin	0 (0)
Paclitaxel/carboplatin+bevacizumab	10 (25.6)
Paclitaxel/cisplatin+avastin	2 (5.1)
Paclitaxel/carboplatin or Paclitaxel/carboplatin+bevacizumab	4 (10.3)

NACT cycles (n=32)	Number (%)
3	16 (50.0)
4	2 (6.3)
3~4	12 (37.5)
3~6 or 4~6	2 (6.3)

Number of cycles of chemotherapy before re-evaluation in
case of initial non-resectability

2 cycles	1 (2.5%)
3 cycles	38 (95%)
4 cycles	1 (2.5%)



Practice pattern in Taiwan on NACT is similar to in French

Attitude to perform genetic testing

Who would you suggest genetic testing? (multiple choice question). (n=39, 49 answers)	Number (%)
All patients	22 (56.4)
High-risk group (ex: stage III or IV, suboptimal debulking)	37 (94.9)
High-grade serous carcinoma	38 (97.4)
Never suggesting genetic testing	1 (2.6)

- Attitude for genetic testing in Taiwan is similar to in German
- For low-risk group (FIGO I-II nonserous type): 6 (15.4%)



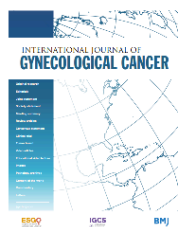
Survey on implementation of molecular testing in ovarian cancer and PARP inhibitor: a national North-Eastern German Society of Gynecologic Oncology/Young Academy of Gynecologic Oncology/Arbeitsgemeinschaft Gynäkologische Onkologie intergroup analysis

Genetic testing population	%
High-grade serous ovarian cancer and FIGO stage III-IV	99.6%
Testing in FIGO stage I-II	78.8%

Appropriate time to perform genetic testing

Timing of genetic testing n=39	Number (%)
Never suggesting genetic testing	1 (2.6)
Newly-diagnosed	32 (82.1)
Newly-diagnosed or recurrence	6 (15.4)

The timing of genetic testing is mostly during newly-diagnosis period. The result is similar to a Germany survey.



Survey on implementation of molecular testing in ovarian cancer and PARP inhibitor: a national North-Eastern German Society of Gynecologic Oncology/Young Academy of Gynecologic Oncology/Arbeitsgemeinschaft Gynäkologische Onkologie intergroup analysis

Timing of genetic testing	%
Pre-operative setting	9.7%
Post-operatively during hospital stay	22.0%
Following the pathology report and tumor board decision	66.5%

What's strategy for genetic testing

- Practice pattern in Taiwan on genetic testing method is similar to a French survey, but different from the Germany survey.

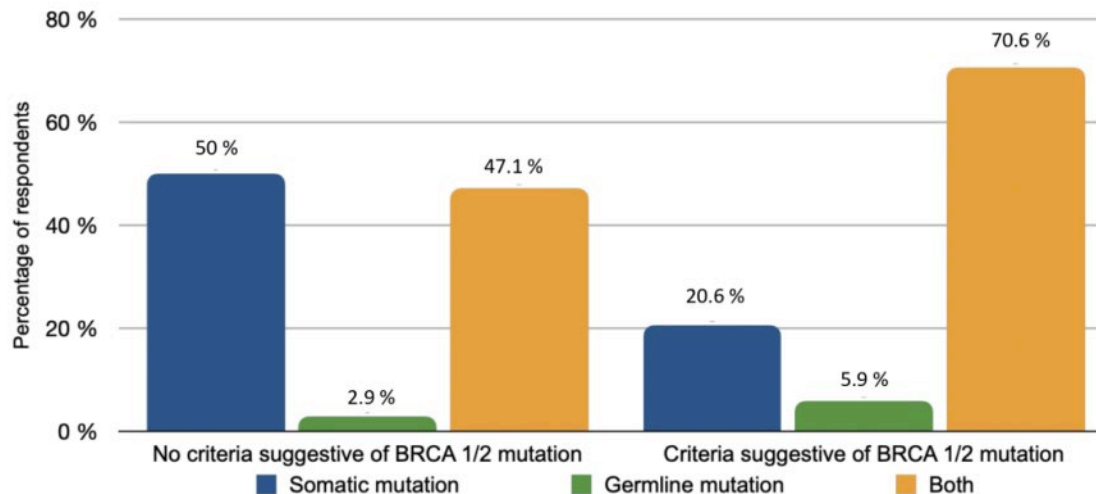
Genetic testing Method (n=38)	Number (%)
Blood	4 (10.5)
Tissue	16 (42.1)
Blood or tissue	18 (47.4)



Article

Results of a 2021 French National Survey on Management of Patients with Advanced Stage Epithelial Ovarian Cancer

Leonor Drouin ¹, Benedetta Guani ², Vincent Balaya ³, Henri Azais ⁴, Sarah Betrian ⁵, Pierre-Adrien Bolze ⁶, Yohann Dabi ⁷, Yohan Kerbage ⁸, Claire Sanson ⁹, François Zaccarini ⁹, Patrice Mathevet ³, Fabrice Lécure ¹⁰, Frédéric Guyon ¹¹, Cherif Akladios ¹², Sofiane Bendifallah ⁷, Elise Deluche ^{13,*} and on behalf of the SFOG Campus (Young of French Society of Gynecological Oncology) [†]



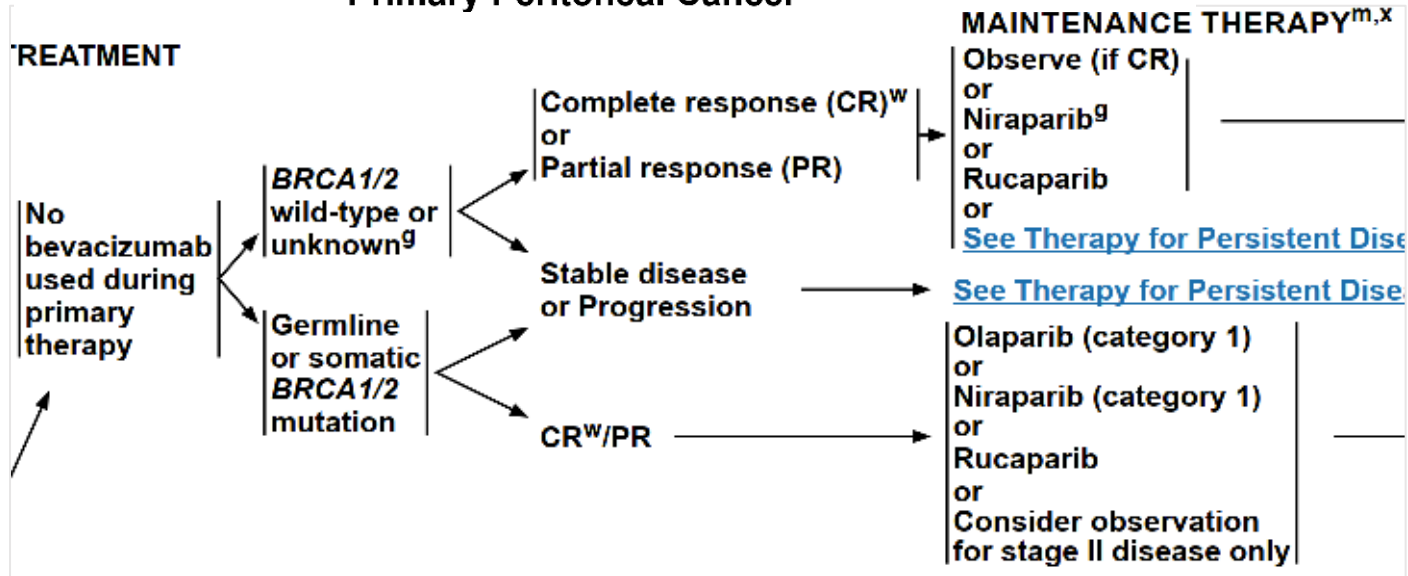
Survey on implementation of molecular testing in ovarian cancer and PARP inhibitor: a national North-Eastern German Society of Gynecologic Oncology/Young Academy of Gynecologic Oncology/Arbeitsgemeinschaft Gynäkologische Onkologie intergroup analysis

Genetic testing Method	%
Blood	21.6%
First do germline testing and if that testing was negative then would add somatic testing	25.1%
Blood and tissue both	25%

Maintenance therapy regimen for the frontline without bevacizumab



NCCN Guidelines Version 2.2023 Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer



BRCA mutation (multiple choice question)	Number (%)
Niraparib	26 (66.7)
Olaparib	36 (92.3)
No maintenance therapy	1 (2.6)
Other	1 (2.6)

BRCA wild-type, HRD (multiple choice question)	Number (%)
Niraparib	35 (89.7)
Olaparib	18 (46.2)
No maintenance therapy	2 (5.1)
Other	2 (5.1)

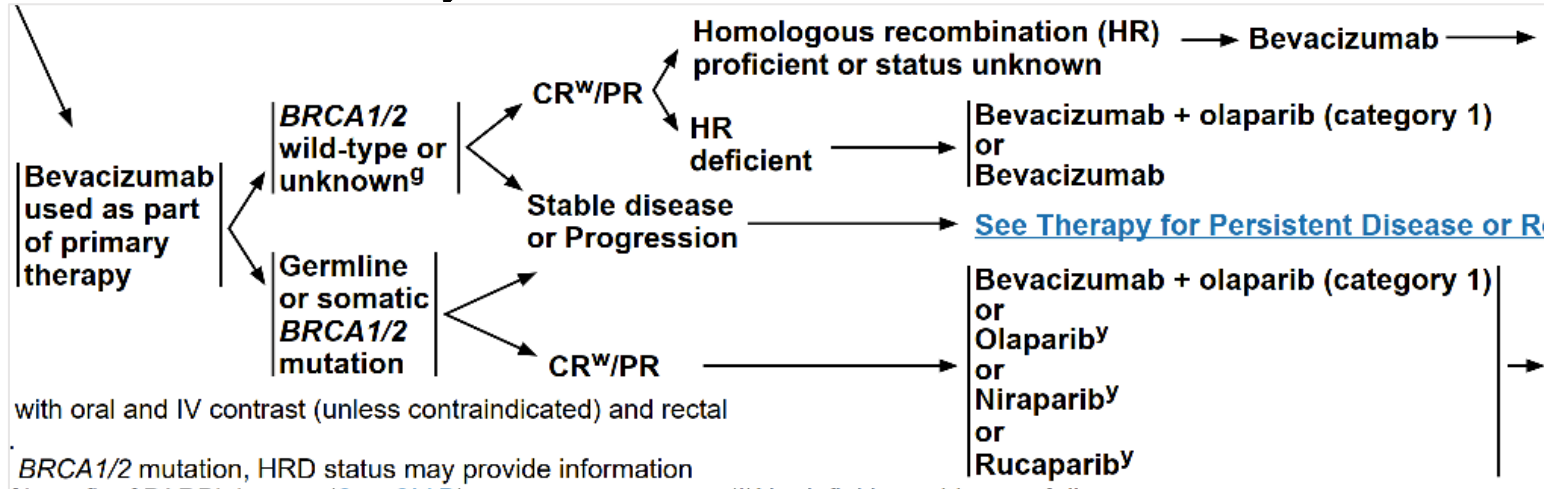
BRCA wild-type, HRP (multiple choice question)	Number (%)
Niraparib	24 (61.5)
Olaparib	6 (15.4)
No maintenance therapy	15 (38.5)
Other	4 (10.3)

NCCN Guidelines Version 2.2023
Epithelial Ovarian
Cancer/Fallopian Tube
Cancer/Primary Peritoneal Cancer

Maintenance therapy regimen for the frontline with bevacizumab



NCCN Guidelines Version 2.2023 Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer



BRCA mutation (multiple choice question)	Number (%)
Niraparib	14 (35.9)
Olaparib	25 (64.1)
Bevacizumab	9 (23.1)
Bevacizumab+ Olaparib	27 (69.2)
No maintenance therapy	1 (2.6)

BRCA wild-type, HRD (multiple choice question)	Number (%)
Niraparib	22 (56.4)
Olaparib	8 (20.5)
Bevacizumab	15 (38.5)
Bevacizumab+ Olaparib	28 (71.8)
No maintenance therapy	1 (2.6)

BRCA wild-type, HRP (multiple choice question)	Number (%)
Niraparib	18 (47.4)
Olaparib	2 (5.3)
Bevacizumab	31 (81.6)
Bevacizumab+ Olaparib	7 (18.4)
No maintenance therapy	3 (7.9)

NCCN Guidelines Version 2.2023
Epithelial Ovarian
Cancer/Fallopian Tube
Cancer/Primary Peritoneal Cancer

Outline

- ◆ The frontline therapy of epithelial ovarian cancer (EOC)
- ◆ The perspective of Taiwan gynecologic oncologists
- ◆ **Oregovomab background**
- ◆ Oregovomab development status
- ◆ FLORA-05 study and FLORA-06 study
- ◆ Take Home Message

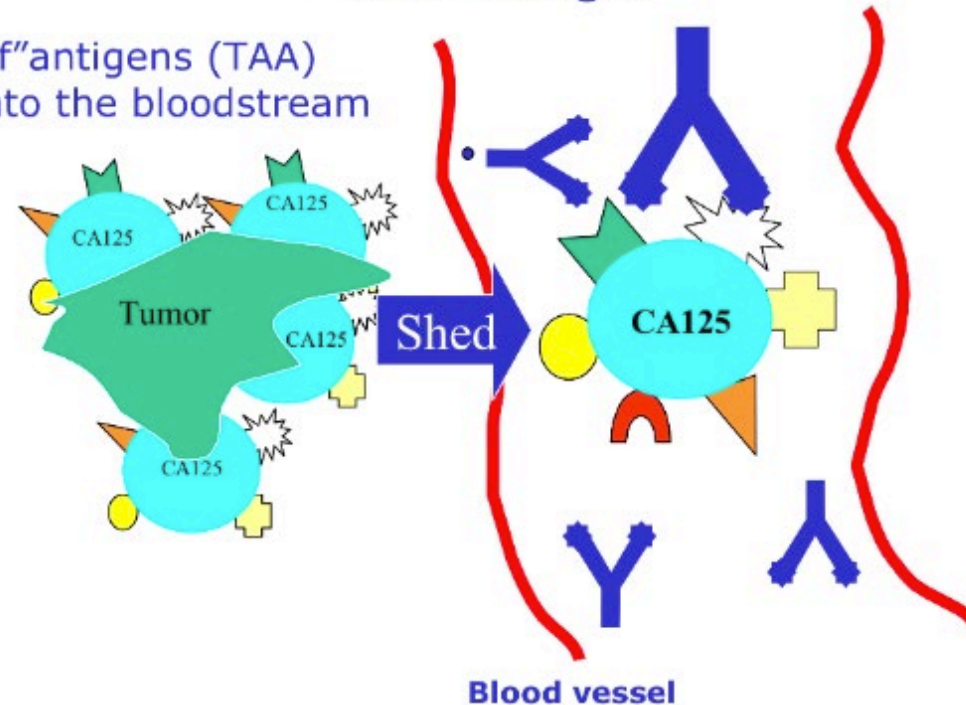
Oregovomab Background

- **CA125:**
 - a mucin-type-O-linked glycoprotein coded by MUC16
 - a suppressor of the anti-tumor immune response
 - expressed in 80% of the EOC cells
 - Anti-CA125 Abs: OC125-like (group A, containing 4 types), M11-like2 (group B), Ov197-like
- OvaRex monoclonal antibody [MAb]-B43.13; A murine (Unither Pharmaceuticals, Wellesley Hills, MA)
- Mab-B43.13 binds with high affinity ($1.16 \times 10^{10}/M$) to CA-125.
- Oregovomab form immunogenic complex with CA-125
 - processed to APCs, such as dendritic cells and macrophages
 - Anti-CD125 Ab and CA-125 specific B and T cell response
 - CD4 and CD8 T-cell responses specific for B43.13.

Immune activation of Oregovomab-1

Oregovomab MAb B43.13 Foreign Antibody Binds to the “Self”-Antigen

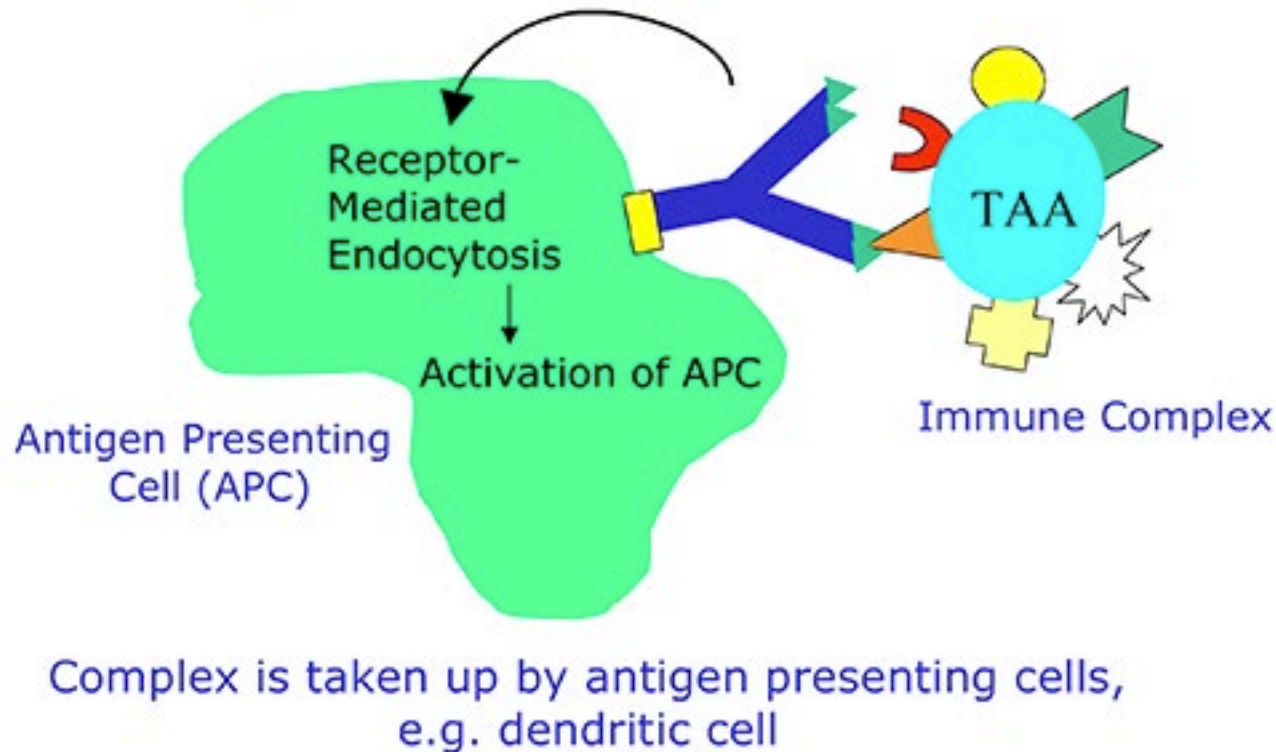
Tumor “self”antigens (TAA) are shed into the bloodstream



Injected low-dose foreign antibody binds TAA and forms immunogenic complex

Immune activation of Oregovomab-2

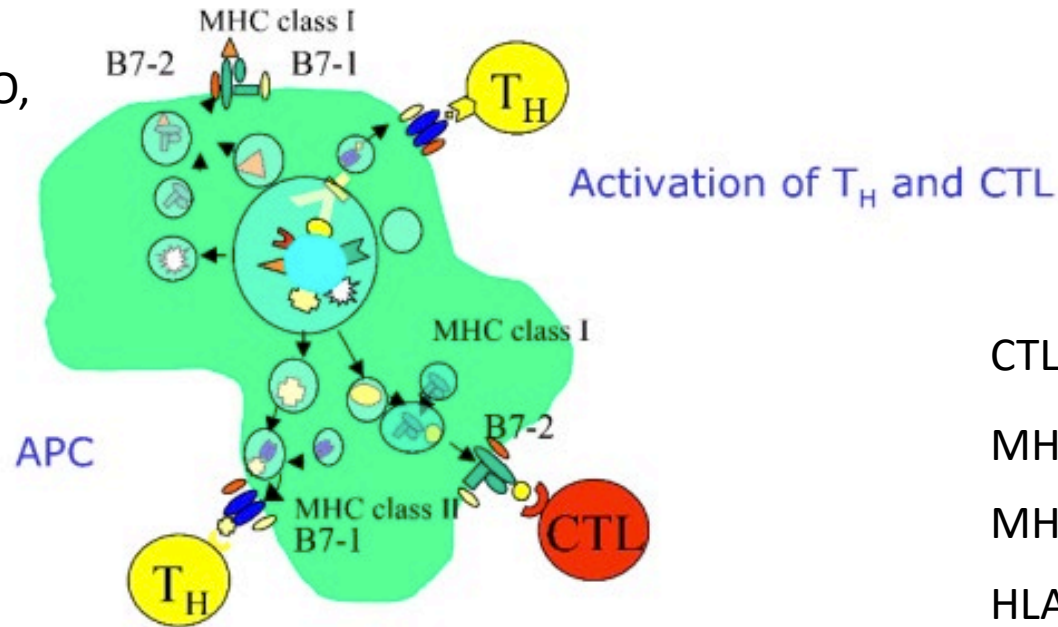
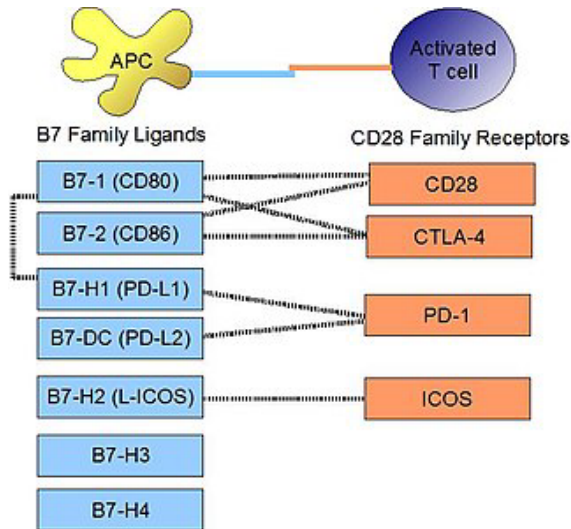
**Oregovomab MAb B43.13- CA125
Complex Binds
Antigen Presenting Cell**



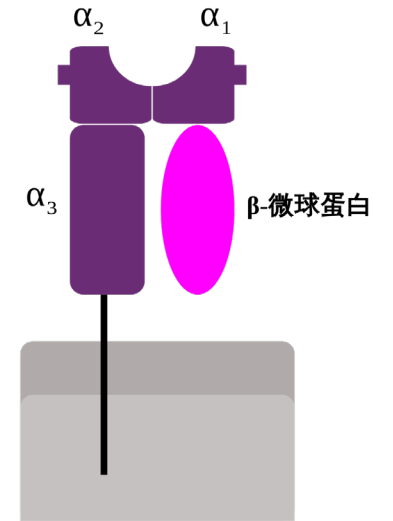
Immune activation of Oregovomab-3

Altered Processing and Activation of Antigen Presenting Cell

MHC class II: HLA-DP, HLA-DM, HLA-DO, HLA-DQ, HLA-DR



Complex is processed and presented on MHC class I and II, B7-1 and B7-2 are up-regulated as a result of complex internalization



CTL (CD8+T): cytotoxic T lymphocyte

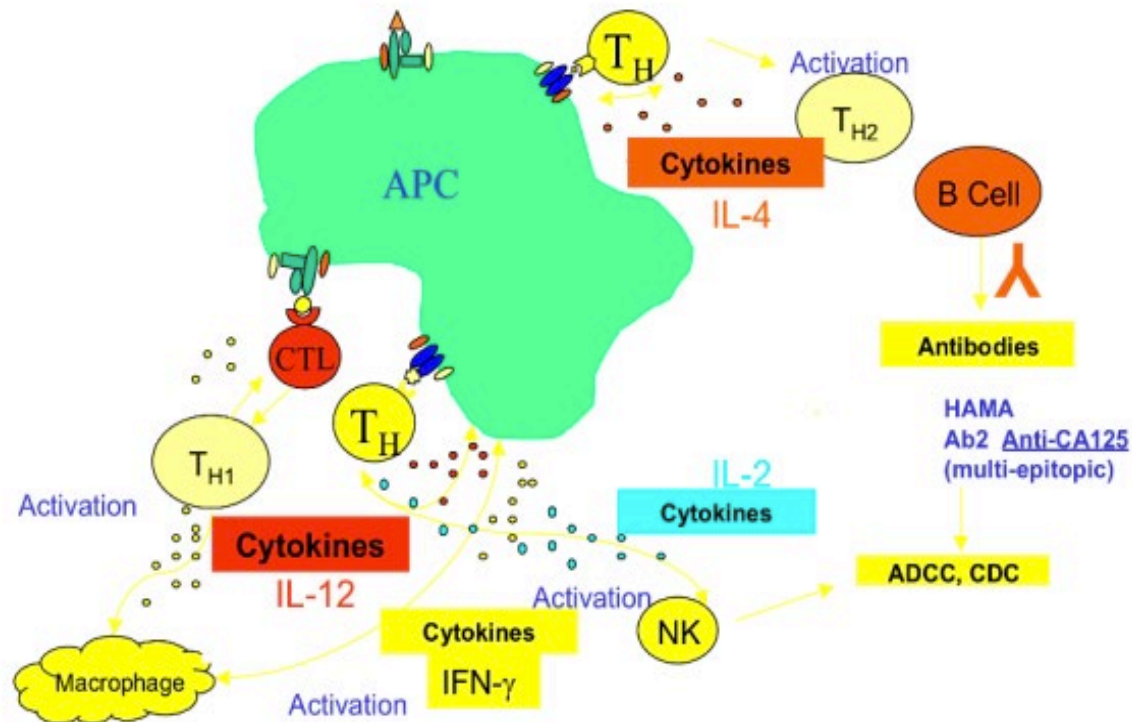
MHC: Major histocompatibility complex

MHC class I: HLA-A, HLA-B, HLA-C

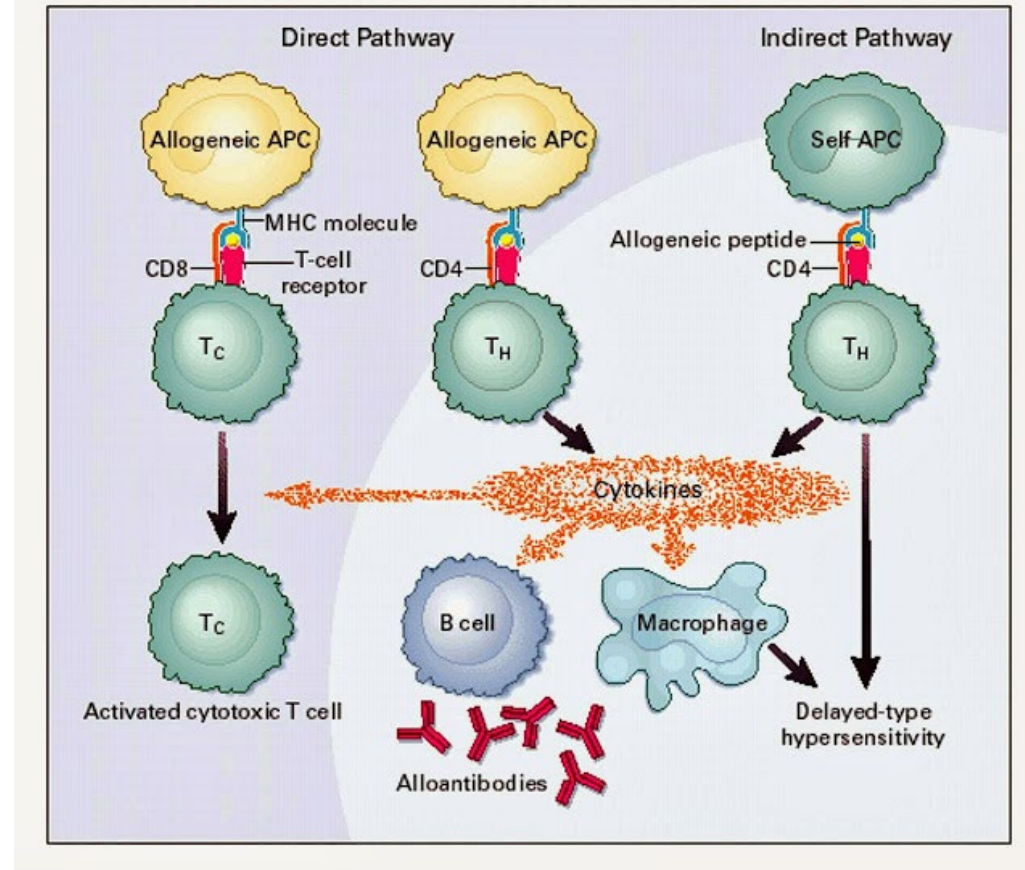
HLA: human leukocyte antigen

Immune activation of Oregovomab-4

Induction of T Helper Cells and CTL



Activation of multiple arms of the immune system



Outline

- ◆ The frontline therapy of epithelial ovarian cancer (EOC)
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- ◆ Oregovomab background
- ◆ **Oregovomab development status**
- ◆ FLORA-05 study and FLORA-06 study
- ◆ Take Home Message

The first study found oregovomab inducing tumor regression in 1993

HYBRIDOMA
Volume 12, Number 5, 1993
Mary Ann Liebert, Inc., Publishers

Clinical Course of Ovarian Cancer Patients Under Repeated Stimulation of HAMA Using MAb OC125 and B43.13

R.P. BAUM,¹ A.A. NOUJAIM,² A. NANJI,¹ V. MOEBUS,¹
A. HERTEL,¹ A. NIESEN,¹ B. DONNERSTAG,¹
T. SYKES,² G. BONIFACE,² and G. HÖR¹

¹Department of Nuclear Medicine of the University of Frankfurt, Frankfurt, Germany
²BIOMIRA INC., Edmonton, Canada

*HAMA=human antimouse antibody

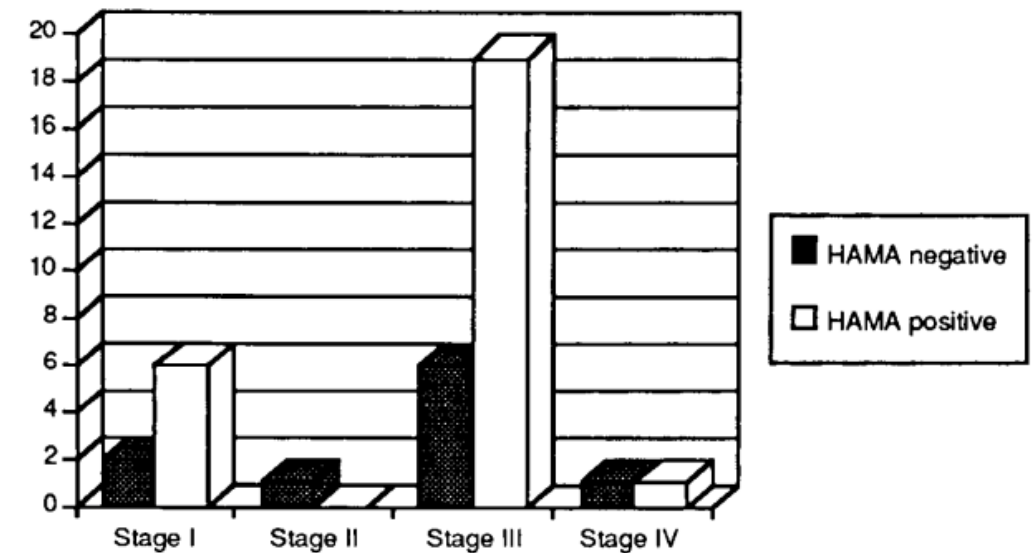


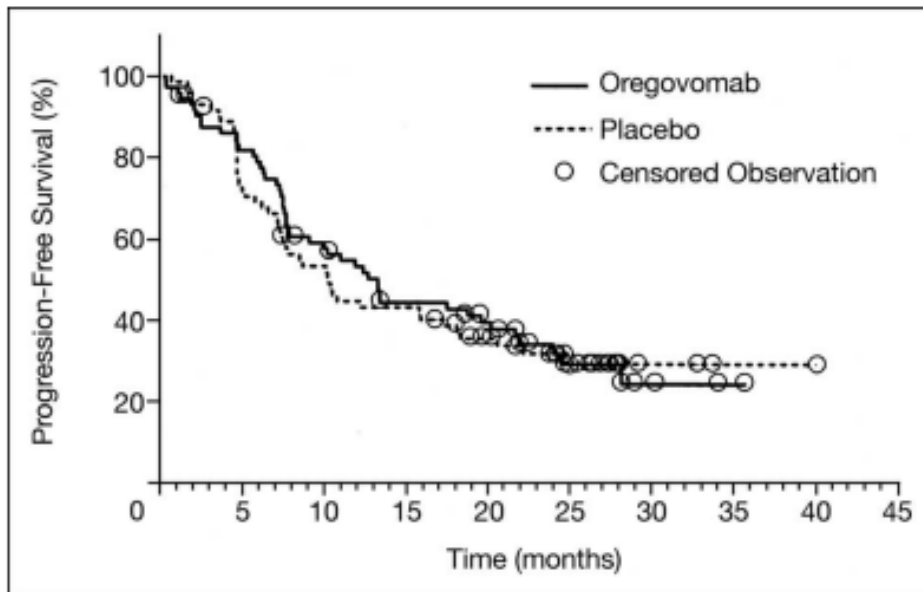
Fig. 5: HAMA Responsiveness in living patients according to their primary tumor stage.

Randomized, Placebo-Controlled Study of Oregovomab for Consolidation of Clinical Remission in Patients With Advanced Ovarian Cancer

Jonathan S. Berek, Peyton T. Taylor, Alan Gordon, Mary J. Cunningham, Neil Finkler, James Orr Jr, Saul Rivkin, Birgit C. Schultes, Theresa L. Whiteside, and Christopher F. Nicodemus

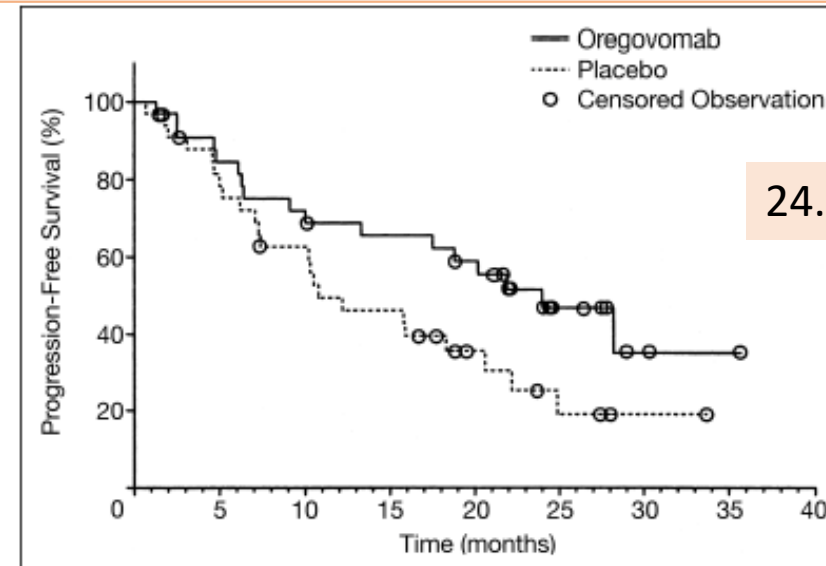
- Phase II trial
- Sample size: 145
- Setting: maintenance
- FIGO stage III or IV

PFS was not different in intention-to-treat.



Favorable PFS in SFLT (successful front-line therapy population).

*SFLT: residual tumor <2cm, favorable response to chemotherapy, normalized but measurable CA-125



24.0 m/o vs. 10.8 m/o

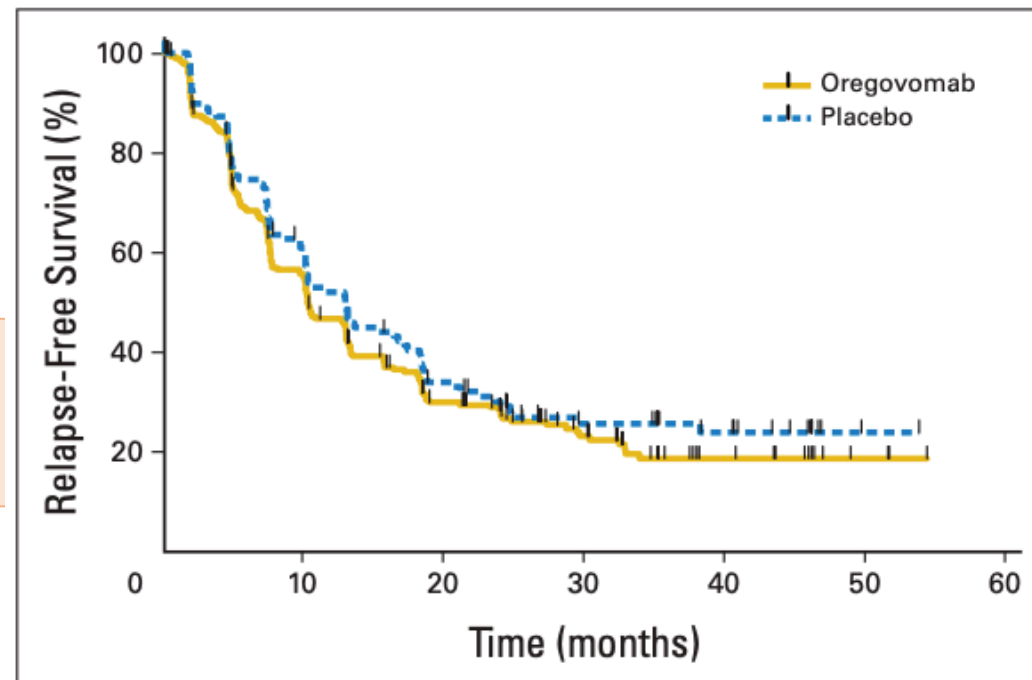
J Clin Oncol. 2004 Sep 1;22(17):3507-16.

Oregovomab Maintenance Monoimmunotherapy Does Not Improve Outcomes in Advanced Ovarian Cancer

Jonathan Berek, Peyton Taylor, William McGuire, L. Mary Smith, Birgit Schultes, and Christopher F. Nicodemus

- FIGO stage III or IV
- **<2cm residual tumor or CA-125 $\leq$ 65 before cycle 3 or no evidence of disease after primary treatment completion**
- Phase III trial
- Sample size: 373
- Setting: maintenance

No difference in relapse-free survival between groups

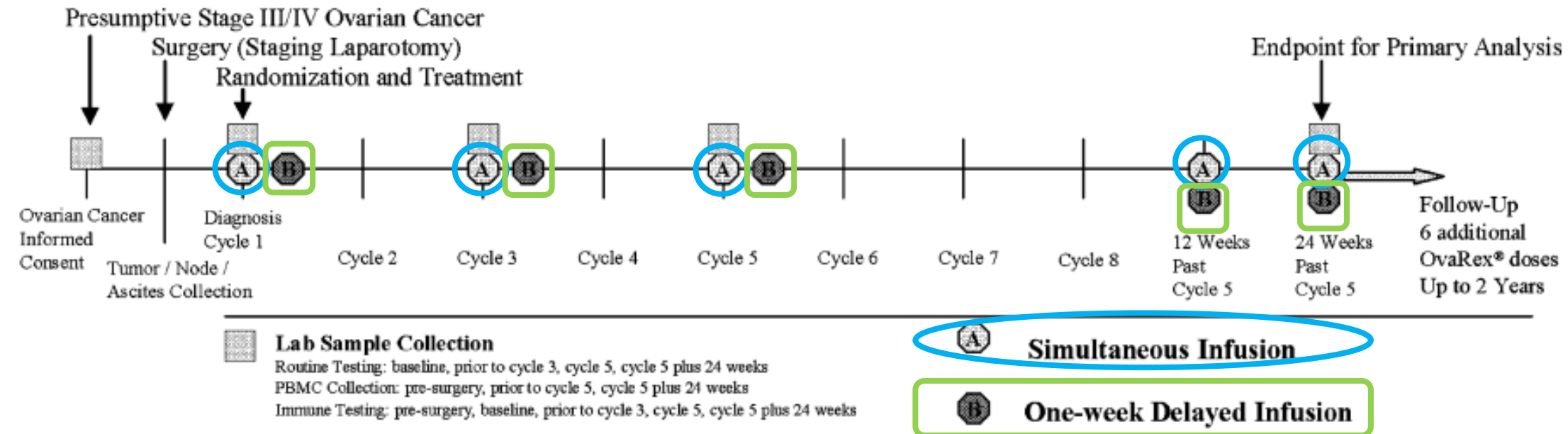


J Clin Oncol. 2009
Jan 20;27(3):418-25.

The Immune Adjuvant Properties of Front-line Carboplatin-Paclitaxel: A Randomized Phase 2 Study of Alternative Schedules of Intravenous Oregovomab Chemoimmunotherapy in Advanced Ovarian Cancer

Patricia Braly,* Christopher F. Nicodemus,† Christina Chu,‡ Yvonne Collins,§ Robert Edwards,|| Alan Gordon,¶ William McGuire,# Christopher Schoonmaker, MS,** Theresa Whiteside, †† Lesley Mary Smith,‡‡ and Michael Method§§

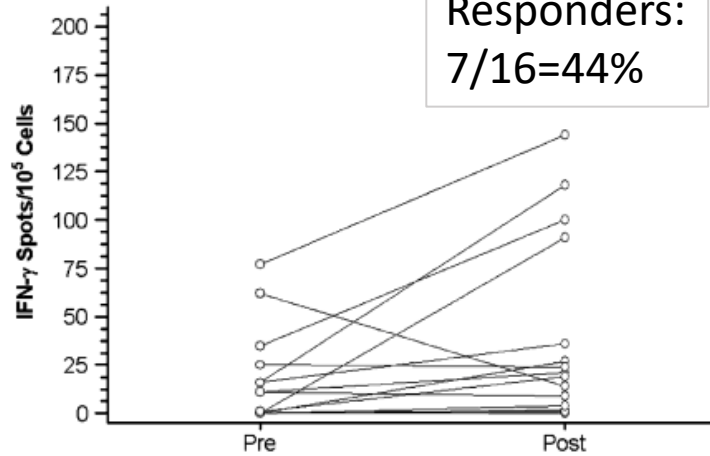
- Phase II trial
- Sample size: 40
- Setting: concomitant or maintenance



J Immunother. 2009 Jan;32(1):54-65.

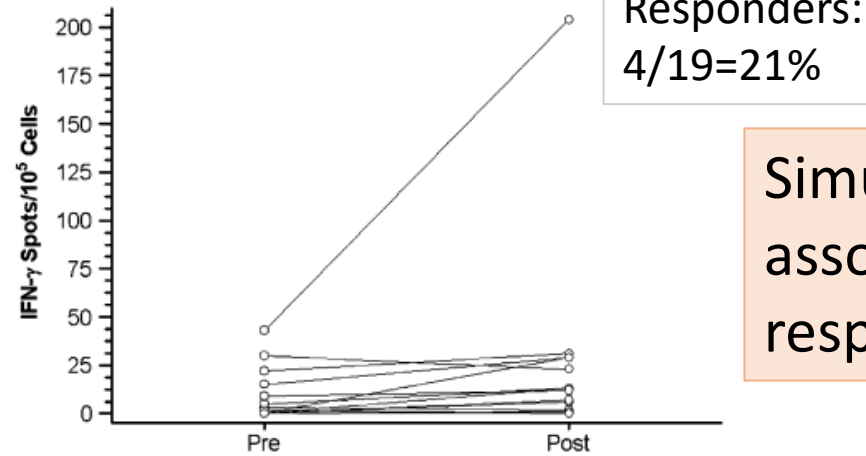
i. Simultaneous Infusion

P=0.04



ii. One-week Delayed Infusion

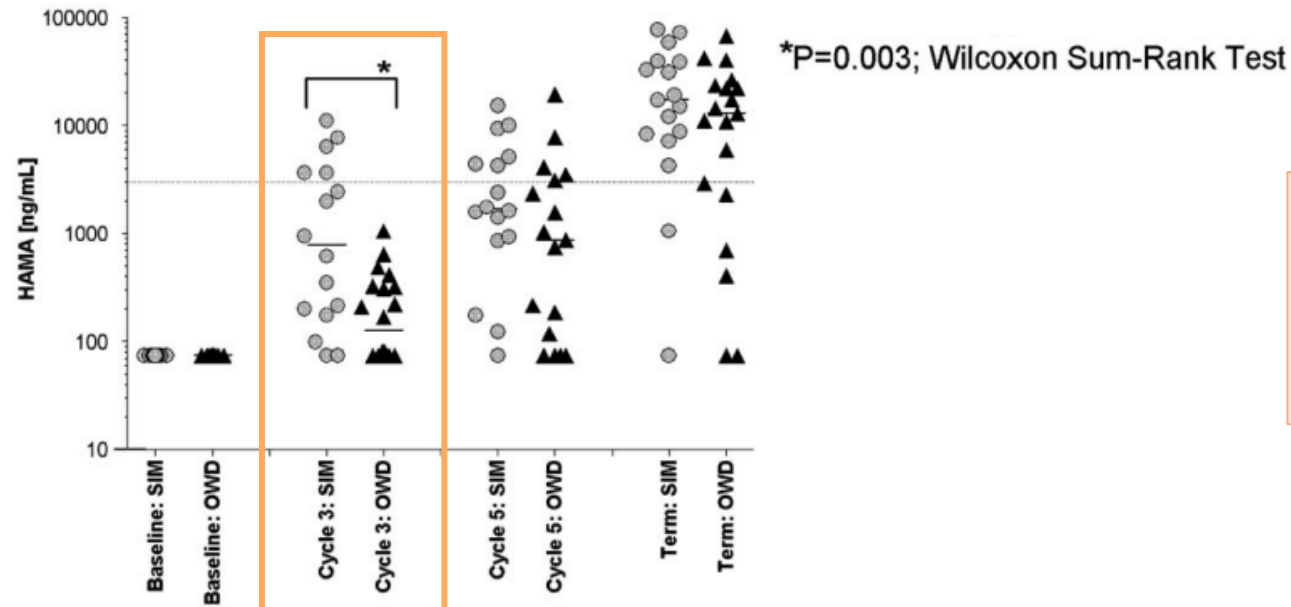
P=0.150



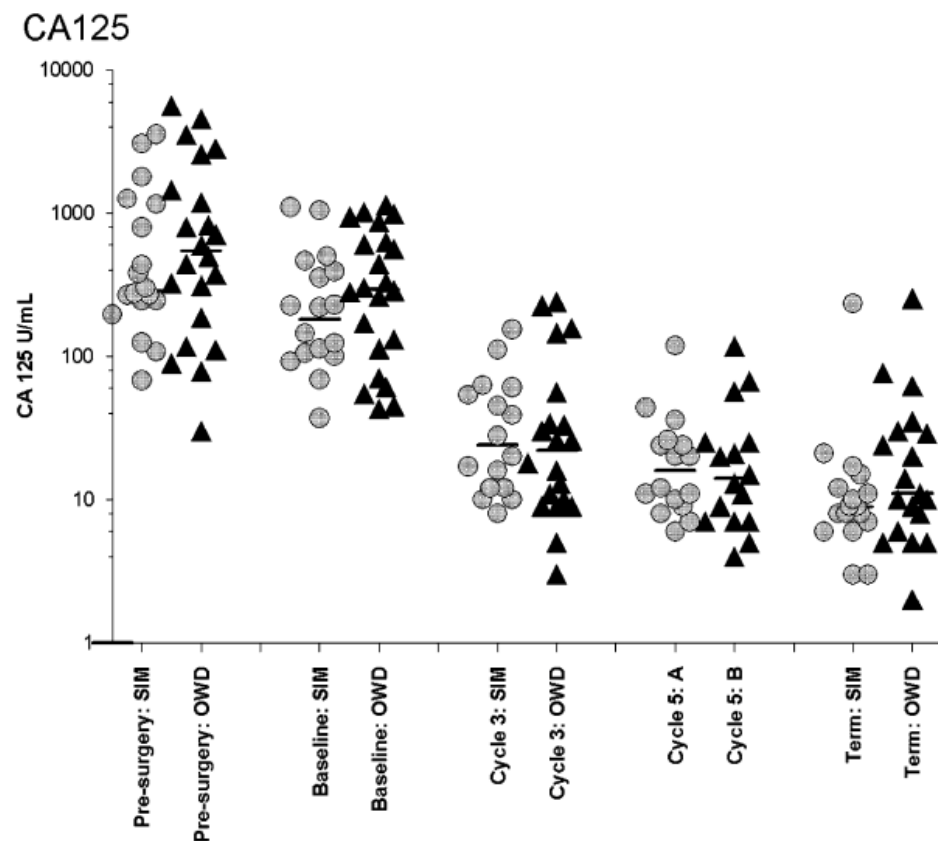
Simultaneous infusion is associated with better T cell response.

B Humoral Immune Responses

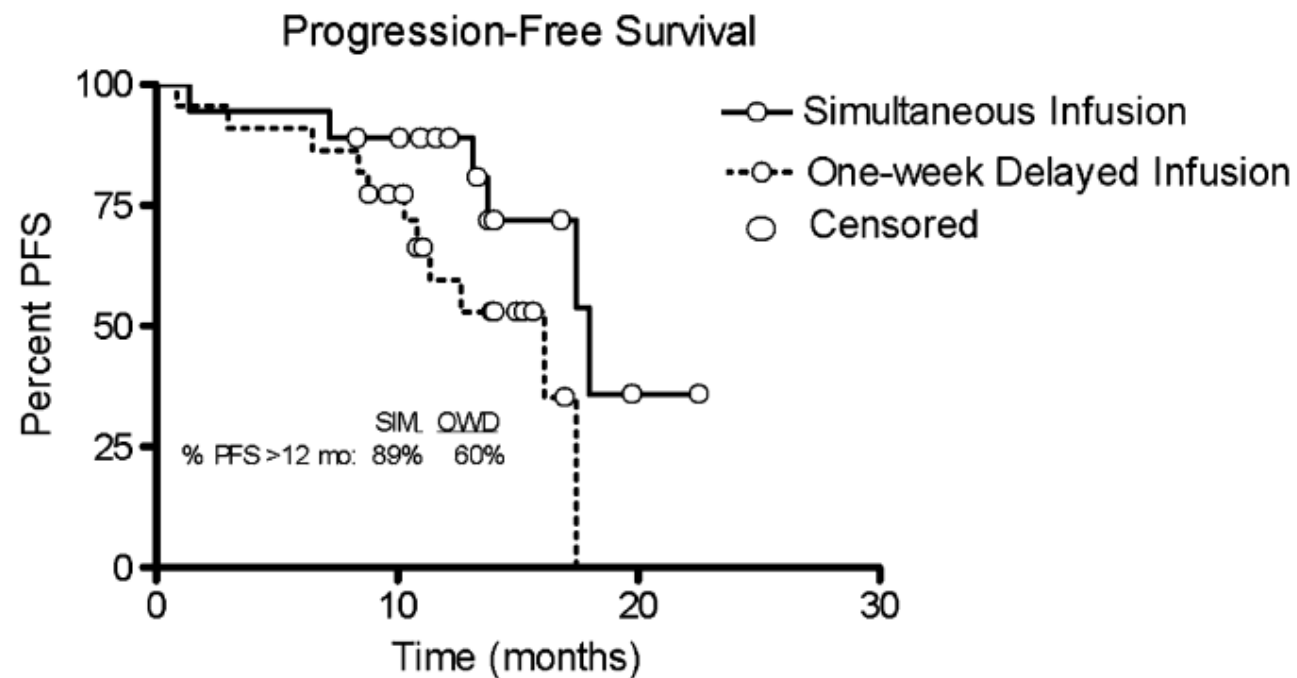
HAMA



Simultaneous infusion is associated with better humoral response.



CA125 dropped rapidly and steadily at the last evaluation in both groups.



Simultaneous infusion had better PFS.

PFS: 17.9 m/o vs. 16.1 m/o

PFS >12 m/o percentage: 89% vs. 60%

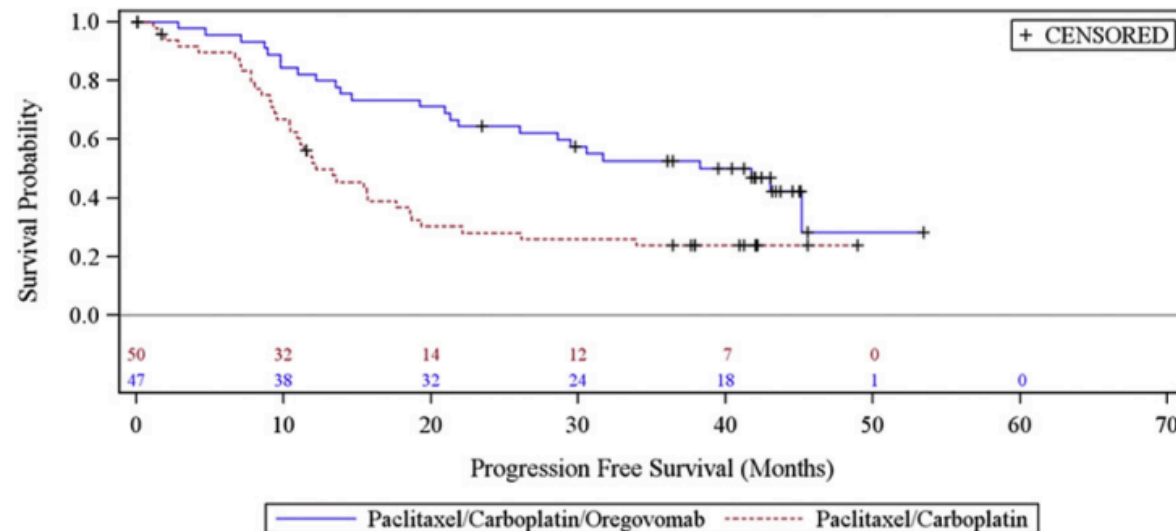
J Immunother. 2009
Jan;32(1):54-65.

- Phase II trial
- Sample size: 97
- Setting: Concomitant first-line
- FIGO stage III or IV

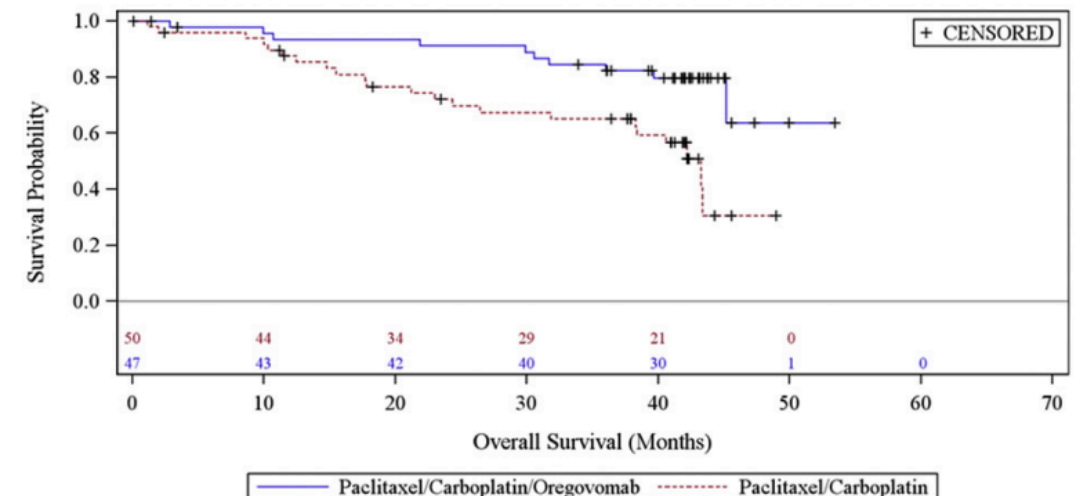
Front-line chemo-immunotherapy with carboplatin-paclitaxel using oregovomab indirect immunization in advanced ovarian cancer: A randomized phase II study☆

Molly Brewer^{a,*}, Roberto Angioli^b, Giovani Scambia^c, Domenica Lorusso^{c,d}, Corrado Terranova^b, Pierluigi Benedetti Panici^e, Francesco Raspagliesi^d, Paolo Scollo^f, Francesco Plotti^b, Gabriella Ferrandina^c, Vanda Salutari^c, Caterina Ricci^c, Patricia Braly^g, Robert Holloway^h, Michael Methodⁱ, Madi Madiyalakan^j, Eliel Bayever^j, Christopher Nicodemus^k

Increased PFS in oregovomab group.
41.8 m/o vs. 12.2 m/o



Increased OS in oregovomab group.
not reached vs. 43.2m/o



Oregovomab safety profile

Table 6. Treatment-Emergent Adverse Events Reported in at Least 10% of Patients in Either Treatment Group

Event*	Oregovomab (n = 249)		Placebo (n = 118)		P
	No.	%	No.	%	
Fatigue	57	22.9	34	28.8	.245
Nausea	49	19.7	34	28.8	.061
Diarrhea	43	17.3	20	16.9	1.000
Abdominal pain	38	15.3	24	20.3	.235
Headache	37	14.9	22	18.6	.364
Arthralgia	36	14.5	18	15.3	.875
Constipation	33	13.3	18	15.3	.629
Back pain	30	12.0	19	16.1	.325
Vomiting	24	9.6	15	12.7	.370
Abdominal distension	21	8.4	12	10.2	.565
Dizziness	19	7.6	11	9.3	.684
Hot flash	17	6.8	13	11.0	.220
Insomnia	21	8.4	9	7.6	1.000
Abdominal pain, lower	22	8.8	7	5.9	.411
Cough	18	7.2	11	9.3	.536
Anxiety	17	6.8	12	10.2	.302

*Medical Dictionary for Regulatory Activities preferred term.

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Oregovomab Maintenance Monoimmunotherapy Does Not Improve Outcomes in Advanced Ovarian Cancer

Jonathan Berek, Peyton Taylor, William McGuire, L. Mary Smith, Birgit Schultes, and Christopher F. Nicodemus

- Phase III trial
- Sample size: 373

No difference in AE between oregovomab or placebo.

TABLE 3. Grade 3/4 Adverse Events ($\geq 5\%$)

List of AE $\geq 5\%$	Simultaneous Infusion		One-week Delayed Infusion		Overall	
	N(%)		N(%)		N(%)	
	AE Grade		AE Grade		AE Grade	
	Grade 3	Grade 4	Grade 3	Grade 4	Grade 3	Grade 4
Abdominal pain	1 (6)	0	0	0	1 (3)	0
Anemia	1 (6)	0	4 (18)	0	5 (13)	0
Arthralgia	1 (6)	0	0	0	1 (3)	0
Constipation	1 (6)	0	0	0	1 (3)	0
Deep vein thrombosis	1 (6)	0	0	0	1 (3)	0
Dehydration	1 (6)	0	1 (4.5)	0	2 (5)	0
Diverticulitis	1 (6)	0	0	0	1 (3)	0
Dyspnea	0	1 (6)	0	0	0	1 (3)
Excoriation	1 (6)	0	0	0	1 (3)	0
Fatigue	1 (6)	0	0	0	1 (3)	0
Febrile Neutropenia	1 (6)	0	1 (4.5)	0	2 (5)	0
Hyperglycemia	1 (6)	0	0	0	1 (3)	0
Hypocalcemia	0	0	2 (9)	0	2 (5)	0
Hypokalemia	0	0	2 (9)	0	2 (5)	0
Hypophosphatemia	0	0	2 (9)	0	2 (5)	0
Migraine	1 (6)	0	0	0	1 (3)	0
Nausea	3 (17)	0	2 (9)	0	5 (13)	0
Neuropathy peripheral	1 (6)	0	0	0	1 (3)	0
Neutropenia	7 (39)	5 (28)	9 (41)	4 (18)	16 (40)	9 (23)
Pain in extremity	1 (6)	0	0	0	1 (3)	0
Pleural effusion	1 (6)	0	0	0	1 (3)	0
Thrombocytopenia	2 (11)	0	2 (9)	2 (9)	4 (10)	2 (5)
Thrombosis	1 (6)	0	0	0	1 (3)	0

AE indicates adverse event.

No difference in AE between simultaneous infusion or delayed infusion.

Oregovomab Development status

Ongoing studies:

1. **Oregovomab and Non-platinum Chemotherapy** in PARP Inhibitor Resistant Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Patients Not Candidate for Platinum Retreatment: a Multicenter, Two-cohort, Single-arm Phase 2 Trial

- Cohort 1: 1 to 3 lines
PLD to be repeated till progression or unacceptable toxicity every four weeks
Investigational agent: Oregovomab at Cycle 1, 2, 3, 5, 7
- Cohort 2: 4 or more lines
Paclitaxel to be repeated till progression or unacceptable toxicity every four weeks on day 1, 8, 15
Investigational agent: Oregovomab at Cycle 1, 2, 3, 5, 7

Status: recruiting

Oregovomab Development status

Ongoing studies:

2. Phase 1b/2, Single Arm Clinical Trial to Evaluate the Safety and Activity of **Oregovomab and Bevacizumab, Paclitaxel Carboplatin** as a Combinatorial Strategy in Subjects With BRCA-wild Type Platinum Sensitive Recurrent Ovarian Cancer

- Single arm
- Intervention:
 - Oregovomab 2 mg on day1 cycle 1, 3, 5, and 9 +
 - Bevacizumab 15mg/Kg Day 1 (every 21 days) until progression +
 - Paclitaxel 175 mg/m², Day 1 x 6 cycles (every 21 days) +
 - Carboplatin AUC 5 IV Day 1 x 6 cycles (every 21 days)
- Primary outcome:
 - Safety and tolerability
 - Overall response rate

Status: recruiting

Oregovomab Development status

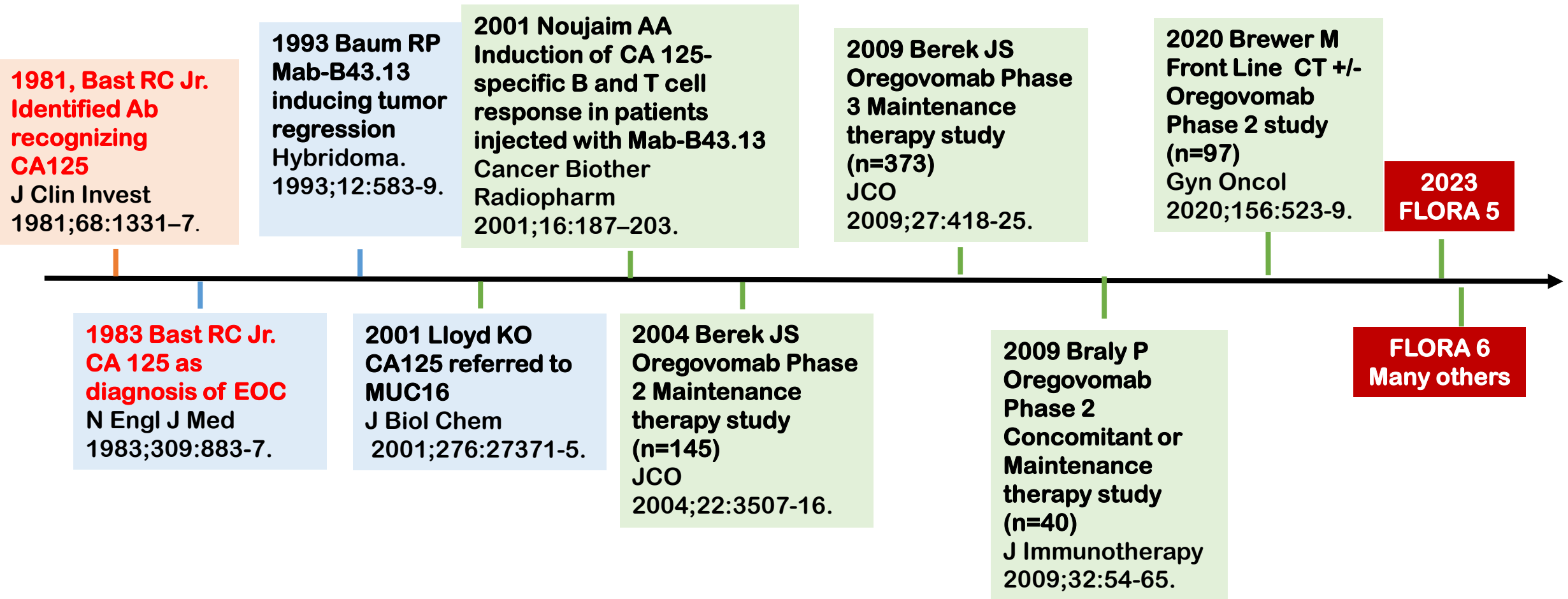
Ongoing studies:

3. A Phase 2, Double-Blind, Placebo-Controlled, Multicenter Clinical Trial Comparing Chemoimmunotherapy (**Paclitaxel-Carboplatin-Oregovomab**) Versus Chemotherapy (Paclitaxel-Carboplatin-Placebo) as Neoadjuvant Therapy in Patients With Advanced Epithelial Ovarian, Fallopian Tube or Peritoneal Carcinoma

- Experimental arm:
 - Six cycles of chemotherapy with oregovomab on cycle 1, 3, 4, 6, and cycle 6 plus 12 weeks
- Placebo arm:
 - Six cycles of chemotherapy with placebo on cycle 1, 3, 4, 6, and cycle 6 plus 12 weeks
- Primary outcome:
 - Progression free survival

Status: recruiting

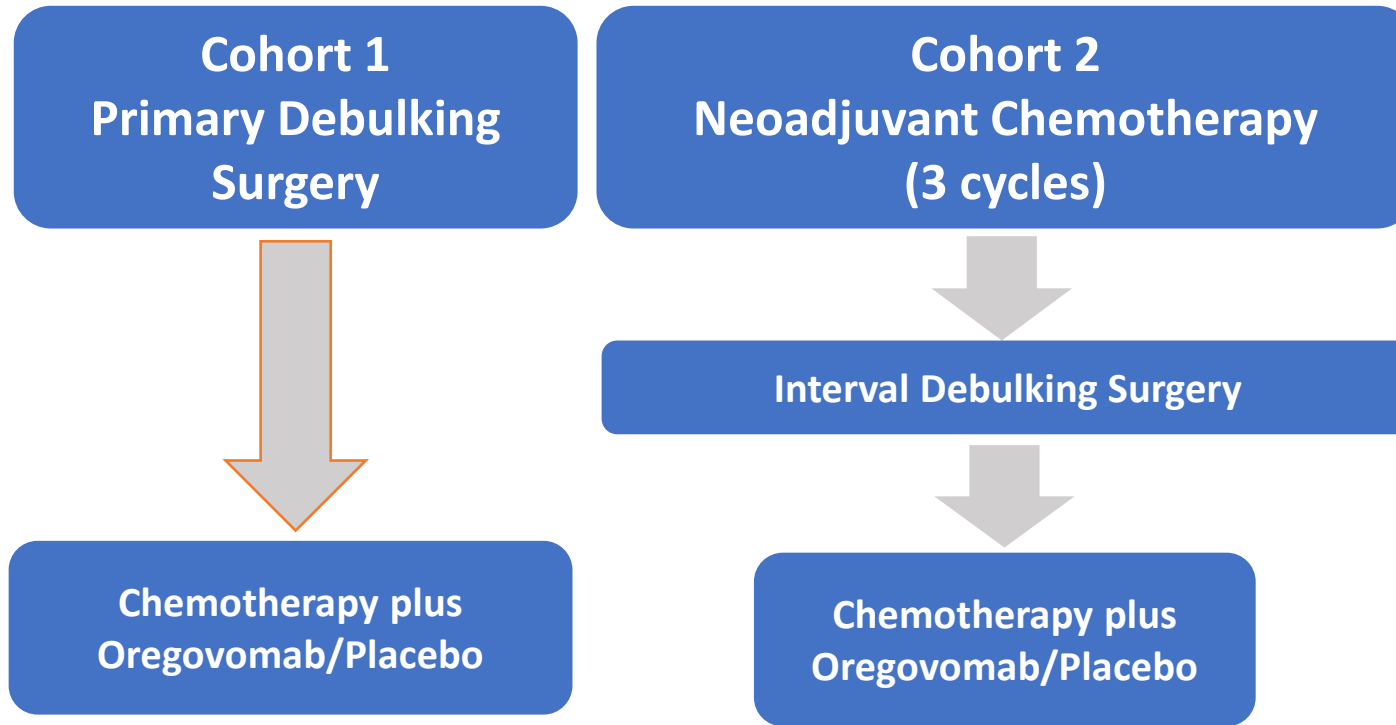
CA125 and Oregovomab Development



Outline

- ◆ The frontline therapy of epithelial ovarian cancer (EOC)
- ◆ The perspective of Taiwan gynecologic oncologists
- ◆ Oregovomab background
- ◆ Oregovomab development status
- ◆ FLORA-05 study and FLORA-06 study
- ◆ Take Home Message

FLORA-5 study. (NCT04498117)



Recruitment completed on 28th June
2023 (N = 618)

Primary End Point:
Progression Free Survival (PFS)

Secondary End Point:
Overall Survival (OS)
Safety and Tolerability
Quality of Life

Exploratory End Point:
Post-progression Outcome
Potential Biomarkers

FLORA-5 protocol

Screening
period



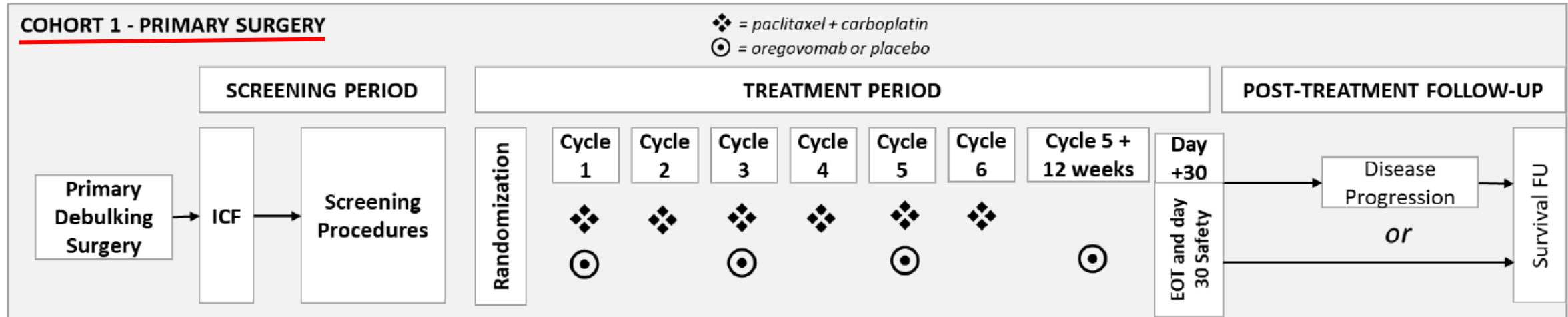
Treatment
period



Post-treatment
follow Up

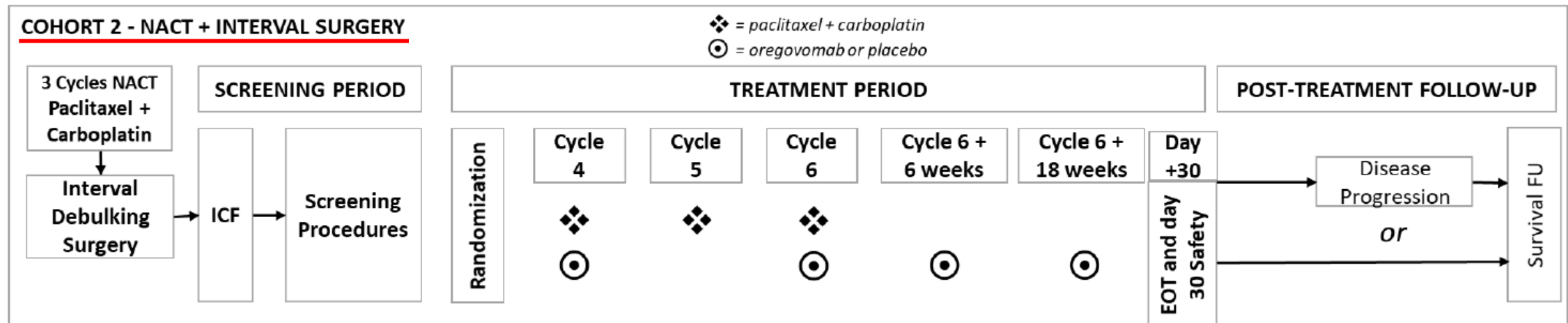
COHORT 1 - PRIMARY SURGERY

❖ = paclitaxel + carboplatin
⊙ = oregovomab or placebo



COHORT 2 - NACT + INTERVAL SURGERY

❖ = paclitaxel + carboplatin
⊙ = oregovomab or placebo



FLORA-5 eligibility criteria

Eligibility criteria

Adults 18 years old or older

Newly diagnosed epithelial adenocarcinoma of ovarian, fallopian tube or peritoneal origin

FIGO Stage III or IV disease

Cell types: high grade serous adenocarcinoma, high grade endometrioid adenocarcinoma, undifferentiated carcinoma, clear cell adenocarcinoma, mixed epithelial carcinoma, or adenocarcinoma not otherwise specified (N.O.S.)

CA-125:

- Cohort1 (primary surgery): Preoperative serum CA-125 levels ≥ 50 U/mL
- Cohort2 (NACT + interval surgery): serum CA-125 levels ≥ 50 U/mL prior to 1st NACT

For women of childbearing potential, must be willing to avoid pregnancy by using a highly effective method of contraception from the first dose of study treatment to 6 months after last dose of study treatment.

Completed debulking surgery (primary debulking surgery or interval debulking surgery at the discretion of the investigator)

Inclusion Laboratory Values

Adequate bone marrow function:

- ANC $\geq 1,500/\mu\text{L}$
- Platelets $\geq 100,000/\mu\text{L}$
- Hemoglobin ≥ 8.0 g/dL

Adequate liver function:

- Bilirubin $< 1.5 \times \text{ULN}$
- LDH, SGOT/AST and SGPT/ALT $< 2.5 \times \text{ULN}$

Adequate renal function:

- Creatinine $\leq 1.5 \times \text{ULN}$

FLORA-5 exclusion criteria

Exclusion criteria

BRCA1 or BRCA2 germline gene mutation test result with:

- **Pathogenic, ambiguous or inconclusive result** available within 28 days prior to starting study treatment. (patients with BRCA1/2 variants of uncertain significance can enroll onto the study if there is no intent to administer PARP inhibitors for front-line maintenance therapy)
- **Known BRCA1 and BRCA2 somatic mutations**

Known **Somatic Homologous Recombination Deficiency (HRD) who will receive PARP inhibitor** front-line maintenance therapy

Cell types: mucinous adenocarcinoma, carcinosarcoma, tumors with neuroendocrine features and low-grade adenocarcinoma

Autoimmune disease

Known allergy to murine proteins or hypersensitivity to any of the excipients of the oregovomab, paclitaxel, or carboplatin

Chronically treated with immunosuppressive drugs

Chronic therapeutic corticosteroid use, defined as > 5 days of prednisone or equivalent, with the exception of inhalers or those on a pre-planned steroid taper.

May not receive any live, attenuated vaccine administered within 28 days prior to enrolment, during the study, and for at least 90 days after the last dose

Other Exclusion Criteria

- **Serious medical or psychiatric illness**
- **Uncontrolled or life-threatening diseases compromising safety evaluation.**
- **Diagnosed or treated for another malignancy within 5 years**
- **Contraindications to the use of pressor agents.**
- **Undergone more than one surgical debulking or have not recovered from surgery.**
- **History or evidence upon physical examination of CNS disease, seizures not controlled with standard medical therapy, or any brain metastases.**
- **Active infection(s) at the time of screening.**
- **Significant cardiovascular conditions**

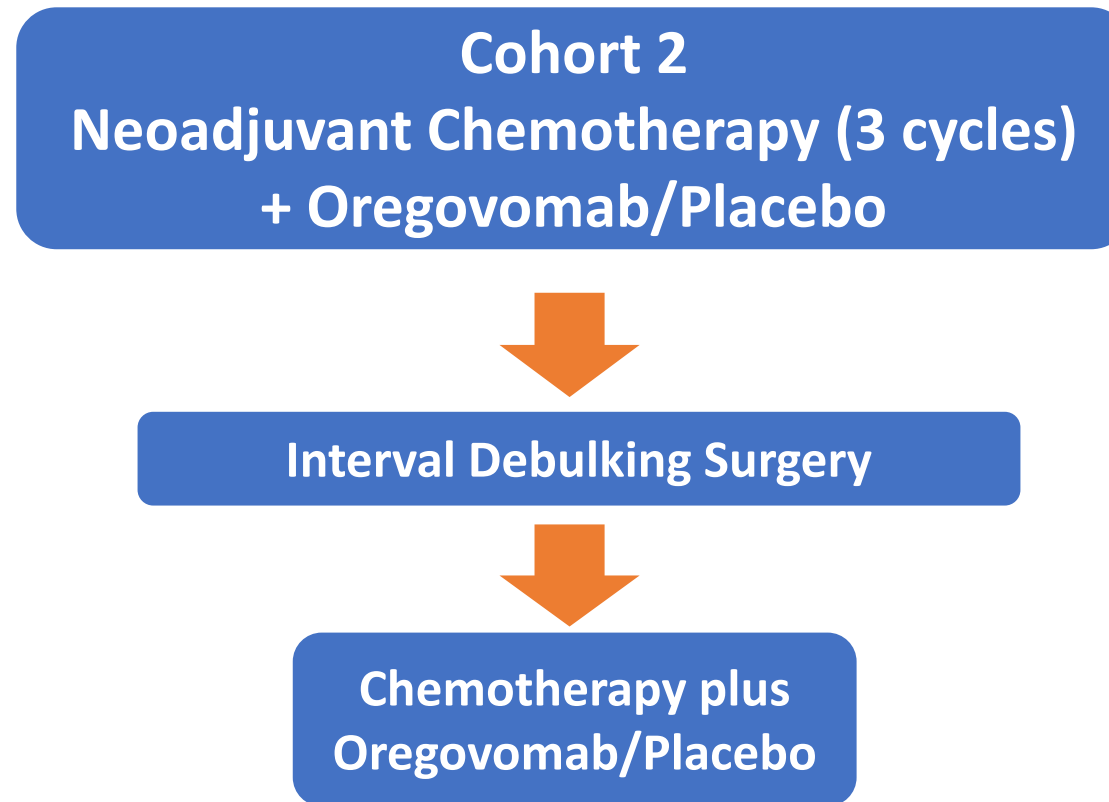
FLORA-5 recruitment in Taiwan

Site	Total Screened	Screening Failure	Total Randomized
15801 NTUH	1	0	1
15802 TPVGH	11	2	9
15803 NCKUH	11	4	7
15804 KFSYSCC	5	1	4
15805 CMUH	0	0	0
15806 TCVGH	11	4	7
Total	39	11	28

- No any grade 3 or grade 4 adverse event developed in TPVGH

FLORA-6 (NCT05605535)

(Recruiting)



Comparison of FLORA-5 and FLORA-6

FLORA-5

Cohort 1
Primary Debulking
Surgery

Cohort 2
Neoadjuvant Chemotherapy
(3 cycles)

Interval Debulking Surgery

Chemotherapy plus
Oregovomab/Placebo

Chemotherapy plus
Oregovomab/Placebo

BRCA + excluded

FLORA-6

Neoadjuvant Chemotherapy
(3 cycles)
plus Oregovomab/Placebo

Interval Debulking Surgery

Chemotherapy plus
Oregovomab/Placebo

All comers

Outline

- ◆ The frontline therapy of epithelial ovarian cancer (EOC)
- ◆ The perspective of Taiwan gynecologic oncologists
- ◆ Oregovomab background
- ◆ Oregovomab development status
- ◆ FLORA-05 study and FLORA-06 study
- ◆ Take Home Message

Take-home messages

- The practice pattern in the management of EOC patients in the front-line status is relatively diverse among gynecologic oncologists in Taiwan.
- It might be due to the treatment uncertainty, poor outcome and high cost of adding extra examination and therapy for EOC patients in Taiwan.
- Immuno-chemotherapy may offer a better chance as choice for front-line therapy in EOC patients, without increasing adverse events and particularly beneficial to those advanced stage and BRCA naïve (or HR intact) patients.
- Many trials are still ongoing to focus on the safety and efficacy of immuno-chemotherapy
- FLORA-5: Investigation of Oregovomab in the setting of primary surgery or neoadjuvant chemotherapy (NACT) with interval cytoreductive surgery in the EOC patient group of negative BRCA mutation.

Thank you for attention!

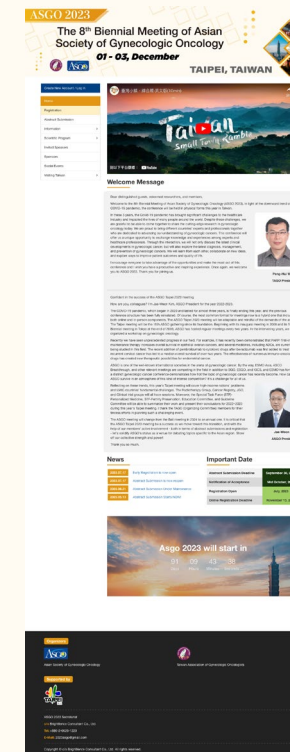


2023

The 8th Biennial Meeting of Asian Society of Gynecologic Oncology



ASGO 2023



<https://www.asgo2023.org/site/page.aspx?pid=901&sid=1511&lang=en>

2023.12.01-12.03

HNBK International Convention Center

TAIPEI

Conference Information

Conference: The 8th Biennial Meeting of
Asian Society of Gynecologic Oncology
(ASGO 2023)

Date: 2023.12.01 (Fri.) ~ 12.03 (Sun.)

Venue: HNBK International Convention Center



Program at a Glance

Time	December 1 (Fri.)				December 2 (Sat.)					December 3 (Sun.)					
Room (Num. of seats)	Main (420)	201 (216)	202 (216)	203 (98)	Main (420)	201 (216)	202 (216)	203 (98)	301 (374)	Main (420)	201 (216)	202 (216)	203 (98)	301 (374)	
0830-0855	Rare Cancer (1) (RC)	STF (Personal Medicine) (AP)	Oral Presentation (1) (OP)	Video Presentation (1) (VP)	Opening Ceremony					Basic Science (BS)	Cancer Registry in Asia (AR)	JGO (AJ) (EB meeting: 8:00am)	Radiotherapy (RA)		
0855-0920					Keynote Speeches (KS)		Tumor Board (1) (TB)								
0920-0945															
0945-1010															
1010-1020	Coffee Break				Coffee Break		Coffee Break								
1020-1045	Rare Cancer (2) (RC)	STF (Fertility Preservation) (AF)	Oral Presentation (2) (OP)	Video Presentation (2) (VP)			Coffee Break		Late-breaking Abstracts Presentation (LB)	Cancer Patient Management (CP)	Immunotherapy (AI)	Guideline (AG)	Genomic & Biomarker or Prognostic Marker (GB)	Tumor Board (2) (TB)	
1045-1110															
1110-1135															
1135-1200															
1200-1250	Young Doctor Session	Lunch Symposium			Lunch Symposium										
1250-1340		Lunch Break			After Lunch Symposium										
1340-1405	Cervical Cancer (1) (CC)	Endometrial Cancer (1) (EC)	Debate (1) (DE)	AI & Database (1) (AD)	Sponsor's Symposium (SSA)	Sponsor's Symposium (SSB)	Clinical Trial Groups in Asia (AT)	Image (1) (IM)	Novel Therapies (NT)						
1405-1430															
1430-1455															
1455-1520															
1520-1550	Coffee Break				Coffee Break										
1550-1615	Cervical Cancer (2) (CC)	Endometrial Cancer (2) (EC)	Debate (2) (DE)	AI & Database (2) (AD)	Surgical Technique (ST)	Ovarian Cancer (OC)	Education (AE)	Image (2) (IM)							
1615-1640															
1640-1705															
1705-1730															
1800-2100	Welcome Party @ 3F Rm301				Gala Dinner @ 3F Rm301										
*The scienfic program is not final and subject to change.															

Keynote Session on December 2

Session	Keynote Speech (KS)
0800-0840	(KS-1) Clinical Implications of New Paradigm in Ovarian Cancer Genesis for Gynecologic Oncologists <u>Ie-Ming Shih, (USA)</u>
0840-0920	(KS-2) Endometrial related topic <u>Charles Leath (USA)</u>
0920-0940	(KS-3) Road to eliminatng cervical cancer in China <u>Li-Hui Wei (China)</u>
0940-1000	(KS-4) The Surge of Endometrial Cancer in China and Approaches for Screening <u>Qin-Ping Liao (China)</u>

About Taipei

Taipei, located in Taiwan's north, is Taiwan's economic, political, and cultural center. It is a modern cosmopolitan metropolis with a lively and diversified face, filled with exuberance. 24-hour convenience stores in almost every few blocks and night markets for late sleepers.



Attractions in Taipei

Taipei Double Decker Sightseeing Bus

<https://www.taipeisightseeing.com.tw/>



Highlights

- Audio guides in five languages.
- Water spray cooling tunnel.
- Tour with 360° panoramic view.
- Free wifi on board.
- AC and open-air seats on second storey deck.

National Chiang Kai-shek Memorial Hall



National Chiang Kai-Shek Memorial Hall is located in the heart of Taipei City. This memorial hall was built in memory of Chiang Kai-shek, the first president of the Republic of China. The memorial hall is white with a blue roof, representing the dominant colors in the ROC flag. As a whole, the colors of blue, white and red express the National Flag and the spirit of freedom, equality and brotherhood. The great building has become a landmark of Taipei City, and it is the attraction most visited by foreign tourists.

National Palace Museum

The Taipei National Palace Museum is a world-class museum that hosts an eclectic collection of treasures kept by generations of Emperors ruling from the Forbidden City. The museum is home to hundreds of thousands of historical relics that make up the world's most comprehensive and precious collection of ancient Chinese artifacts. The entire collection covers 5,000 years of China's historical and artistic achievements. The museum provides Chinese, English, French, German, Japanese, Spanish and Korean language guides and museum-related literature. The museum is a must-see on any visitor's itinerary.



Food in Taipei

For travelers who like good eating, Taipei is a foodie paradise. It is said that, on any street in Taiwan, if you walk three steps, there is a small food shop. Upon walking five steps, you shall bump into a restaurant.

In CNN's 2015 report on a vote by travelers from around the world on their favorite Taiwan foods, braised pork rice was no. 1, beef noodles no. 2, oyster omelets no. 3, and pearl milk tea (bubble tea) no. 4. Other treasures on the list were xiaolongbao (steamed dumplings), pepper bun, popcorn chicken, fried chicken fillet, stinky tofu, danzai noodles, BBQ corn, mango shaved ice,



Taiwan Culture Night

Welcome Party

Join us for Taiwan Night at our Welcome Party!

Indulge in Unique Roadside Banquets, enjoy Electric-Techno
Neon Gods and Chinese Calligraphy, and experience a night
of food, fun, and culture



Dough modeling



Electric-Techno Neon Gods



Chinese Calligraphy



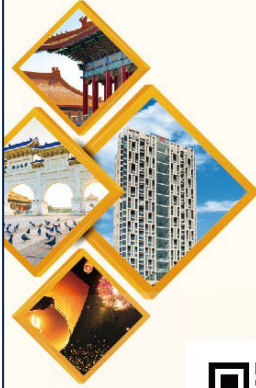
Jazz Party Night

Immerse yourself in the captivating sounds of sultry melodies and smooth rhythms as you socialize with other guests at our vibrant welcome party. Experience the exhilarating energy of Taiwan's most talented musicians as they grace the stage and deliver a stunning live jazz performance that will leave you spellbound.

Our evening banquet presents a scrumptious array of dishes expertly crafted with care and precision. You can savor savory appetizers, mouthwatering main courses, and a tempting selection of desserts, all in an unforgettable dining experience.



- Dress Code : Formal



The 8th Biennial Meeting of Asian Society of Gynecologic Oncology



Official Website

Registration & Abstract Submission is OPEN NOW!



Important Date

Abstract Submission Deadline	September 30, 2023
Notification of Acceptance	Mid October, 2023
Online Registration Deadline	November 15, 2023

TAIPEI

2023

12.01-12.03

HNBK
International
Convention Center

**Hope to see you in Taipei on
1 December 2023!**