Current GOG-P Clinical Trials: Ovarian

David O’Malley, M.D.

Ovarian Cancer - Clinical Trial Advisor

GOG Partners

Director, Division of Gyn Oncology
Professor, Department of OB/Gyn
The Ohio State University
James CCC

Active and Upcoming Trials

OVARY			
Front-line neoadjuvant	GOG-3035/FLORA-5	A randomized controlled study of the effectiveness of neoadjuvant chemotherapy (carboplatin and paclitaxel) versus chemo-immunotherapy (carboplatin, paclitaxel and oregovomab) in patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal carcinoma	Recruiting
Front-line	GOG-3036/KEYLYNK-001	A Randomized Phase 3, Double-Blind Study of Chemotherapy With or Without Pembrolizumab Followed by Maintenance With Olaparib or Placebo for the First-Line Treatment of BRCA Non-mutated Advanced Epithelial Ovarian Cancer	Recruiting
Recurrent Low Grade Serous	GOG-3052/VS-6766-201	A Phase 2 Study of VS-6766 (dual RAF/MEK inhibitor) Alone and in Combination with Defactinib (FAK inhibitor) in Recurrent Low-Grade Serous Ovarian Cancer	Recruiting
Low Grade Serous	GOG-3026	A Phase II Trial of Ribociclib (LEE011) plus Letrozole in Women with Recurrent Low-Grade Serous Carcinoma of the Ovary or Peritoneum	Recruiting

Active and Upcoming Trials

OVARY			
Platinum-Resistant	GOG-3018/OVAL	A Randomized, Controlled, Double-Arm, Double-Blind, Multi-Center Study of Ofranergene Obadenovec (VB-111) Combined With Paclitaxel vs. Paclitaxel Combined With Placebo for the Treatment of Recurrent Platinum-Resistant Ovarian Cancer	Recruiting
Platinum-Resistant	GOG-3029/INNOVATE-3	INNOVATE-3: Pivotal, Randomized, Open-label Study of Tumor Treating Fields (TTFields, 200kHz) Concomitant With Weekly Paclitaxel for the Treatment of Recurrent Ovarian Cancer	Recruiting
Platinum-Resistant	GOG-3032/MOONSTONE	A Phase 2 Open-Label, Single-Arm Study to Evaluate the Efficacy and Safety of the Combination of Niraparib and Dostarlimab (TSR-042) in Patients With Platinum-Resistant Ovarian Cancer	Temporarily Closed for Interim Analysis
Platinum-Resistant	GOG-3044/LAE002INT2001	A Randomized Phase II, Open-Label, Multicenter, Parallel Two Arm Study of Afuresertib Plus Paclitaxel and Afuresertib Plus Carboplatin in Patients with Platinum-Resistant Ovarian Cancer	Recruiting
Platinum-Resistant	GOG-3045/MIRASOL	A Randomized, Open-label, Phase 3 Study 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	Recruiting
Platinum-Resistant	GOG-3048/XMT-1536-1	A Phase 1b/2, First-in-Human, Dose Escalation and Expansion Study of XMT-1536 In Patients with Solid Tumors Likely to Express NaPi2b	Recruiting
Platinum-Resistant	GOG-3059	A Phase 3, Randomized, Double-Blind, Adaptive, Placebo/Paclitaxel-Controlled Study of AVB-S6-500 in Combination with Paclitaxel in Patients with Platinum-Resistant Recurrent Ovarian Cancer	Upcoming – Feasibility and site selection ongoing

Ovarian Front-Line

Ovarian

- Front-line
  - **GOG-3035/FLORA-5:** A Multicenter Phase 3, Double-Blind, Placebo-Controlled Study Comparing Chemo-Immunotherapy (Paclitaxel-Carboplatin- Oregovomab) vs Chemotherapy (Paclitaxel-Carboplatin-Placebo) in Patients With Advanced Epithelial Ovarian, Fallopian Tube or Peritoneal Carcinoma (PI: Angeles Alvarez Secord, MD)

    ClinicalTrials.gov Identifier: NCT04498117

  - **GOG-3036/ENGOT-ov43/MK-7339/KEYLYNK-001**: A Randomized Phase 3, Double-Blind Study of Chemotherapy With or Without Pembrolizumab Followed by Maintenance With Olaparib or Placebo for the First-Line Treatment of BRCA Non-mutated Advanced Epithelial Ovarian Cancer (PIs: Robert Coleman, MD and Rebecca Arend, MD)

    ClinicalTrials.gov Identifier: NCT003740165

GOG-3035/FLORA-5

A Multicenter Phase 3, Double-Blind, Placebo-Controlled Study Comparing Chemo-Immunotherapy (Paclitaxel-Carboplatin-Oregovomab) vs Chemotherapy (Paclitaxel-Carboplatin-Placebo) in Patients With Advanced Epithelial Ovarian, Fallopian Tube or Peritoneal Carcinoma

PI: Angeles Alvarez Secord, MD

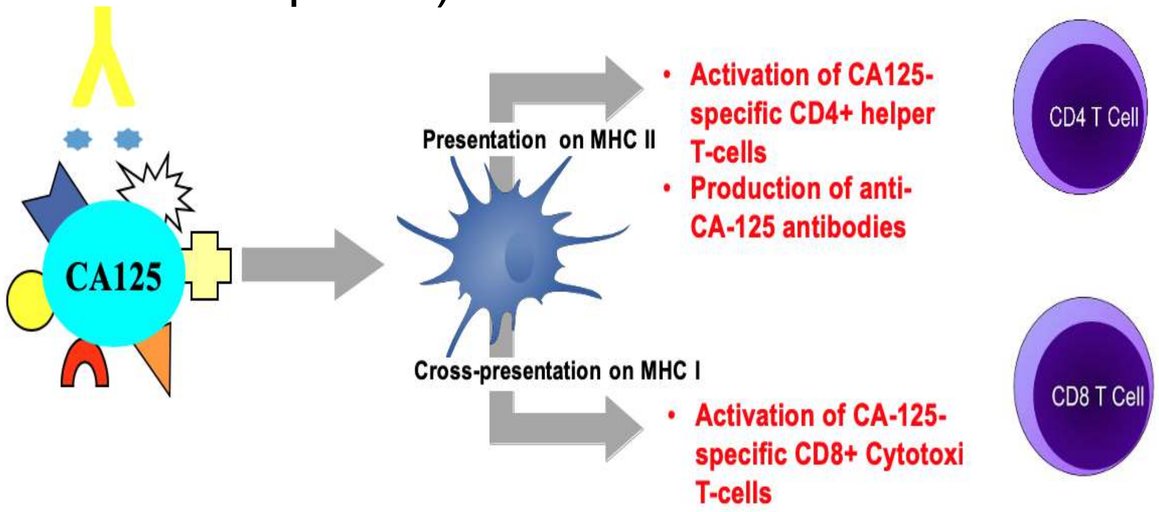
ClinicalTrials.gov Identifier: NCT04498117

GOG-3035/FLORA-5: MOA and Rationale

- Oregovomab: Immunotherapeutic murine monoclonal antibody for ovarian cancers expressing CA-125 (MUC16)

Mechanism of action: Induces immunity by targeting tumor and binding CA-125 rendering it more immunogenic or "neoantigen-like":

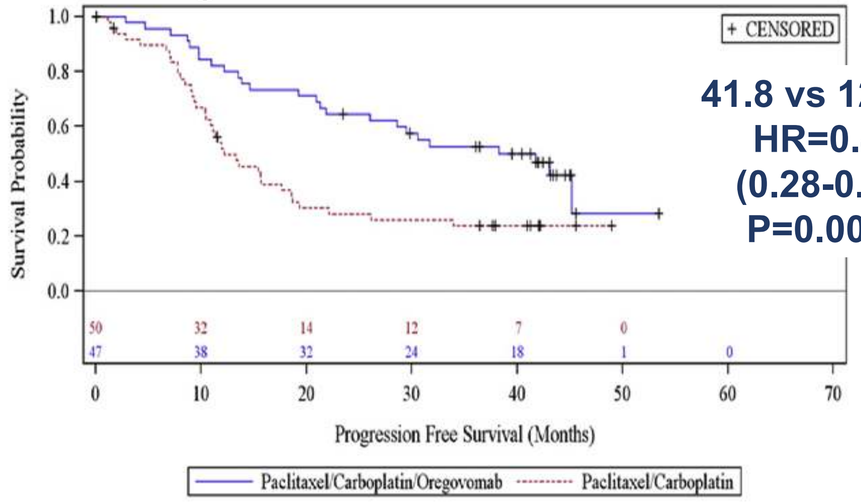
- Processed by antigen presenting cells in circulation and at tissue sites
- Triggers immune responses (interaction with circulating and tissue-associated CA-125 modifies immune response)



1) Gordon A et al., Gynecol Oncol 2004

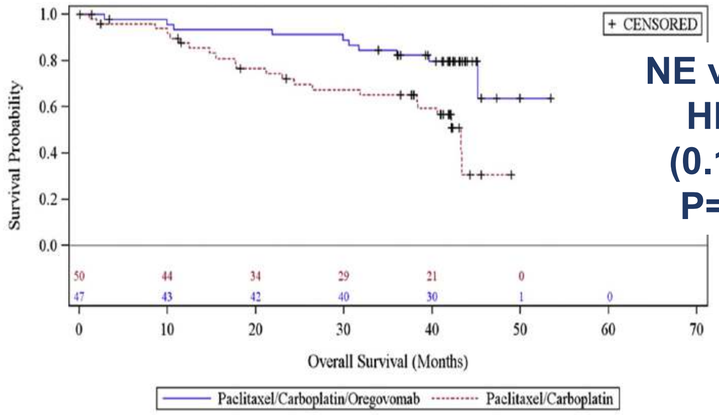
2) Brewer M. et al. Gynecol Oncol 2019

Progression-free Survival



41.8 vs 12.2 m
HR=0.46
(0.28-0.77)
P=0.0027

Overall Survival



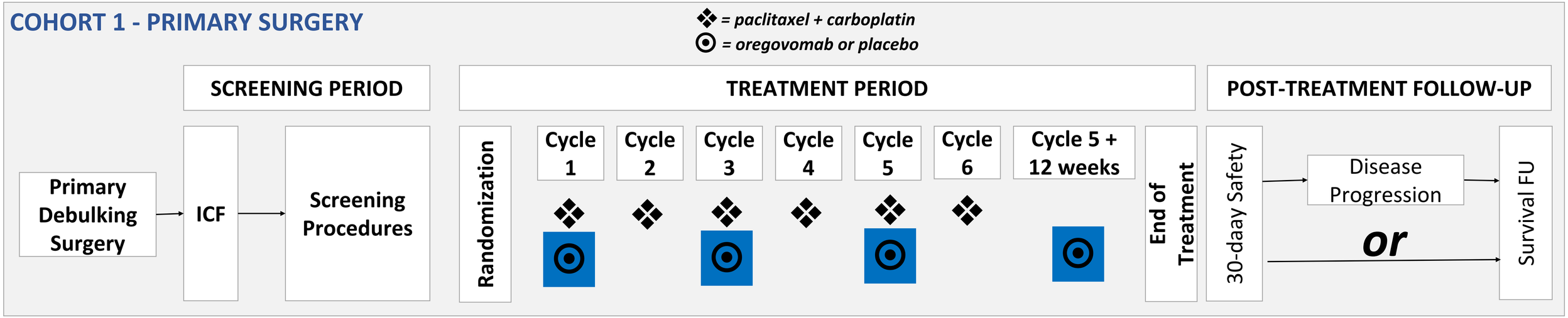
NE vs 43.2 m
HR=0.35
(0.16-0.74)
P=0.0043

GOG-3035/FLORA-5: Schema
Two Cohorts: Primary Surgical and Neoadjuvant

N = 500
GOG Accrual = 7/185
GOG Activated Sites: 23/43
Primary Endpoint: PFS
PI: Alvarez-Secord, A

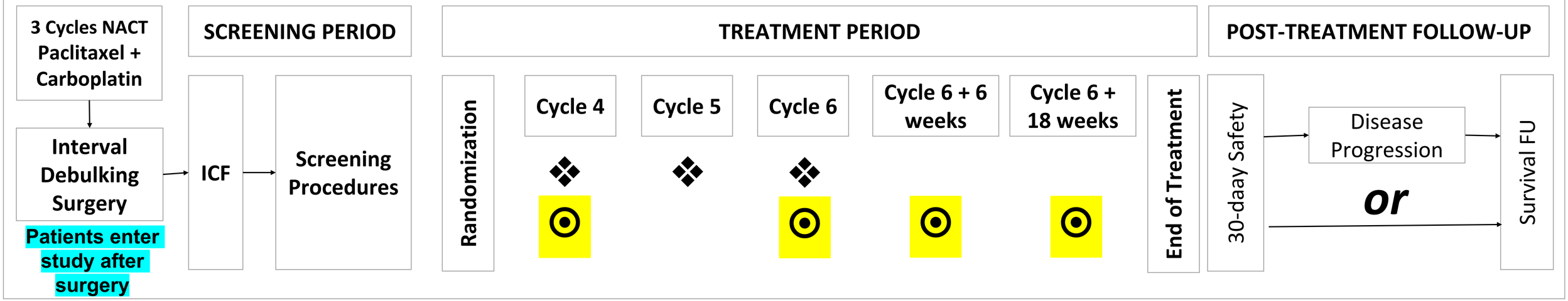
COHORT 1 - PRIMARY SURGERY

❖ = *paclitaxel + carboplatin*
⊙ = *oregovomab or placebo*



COHORT 2 - NACT + INTERVAL SURGERY

❖ = *paclitaxel + carboplatin*
⊙ = *oregovomab or placebo*



GOG-3035/FLORA-5:

Key Eligibility Criteria

- Newly diagnosed epithelial adenocarcinoma of ovarian, fallopian tube or peritoneal origin FIGO Stage III or IV disease.

- Histologic epithelial 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.).

- Completed debulking surgery (either primary debulking surgery or interval debulking surgery at the discretion of the investigator). Debulking surgery must be optimal, R1 or R0 (defined as R1, macroscopic no greater than 1 cm in diameter, or R0, microscopic or no evidence of tumor).

- Preoperative serum CA- 125 levels ≥ 50 U/mL.

GOG-3036/KEYLYNK-001

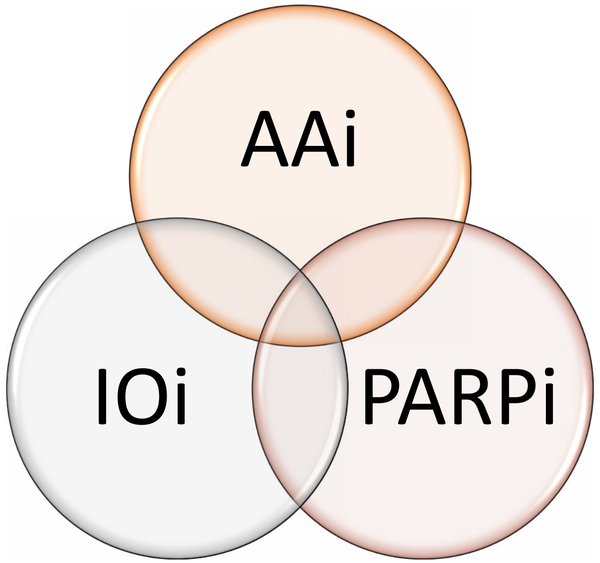
A Randomized Phase 3, Double-Blind Study of Chemotherapy With or Without Pembrolizumab Followed by Maintenance With Olaparib or Placebo for the First-Line Treatment of BRCA Non-mutated Advanced Epithelial Ovarian Cancer (EOC)

PI: Robert Coleman, MD
Co-PI: Rebecca Arend, MD

ClinicalTrials.gov Identifier: NCT003740165

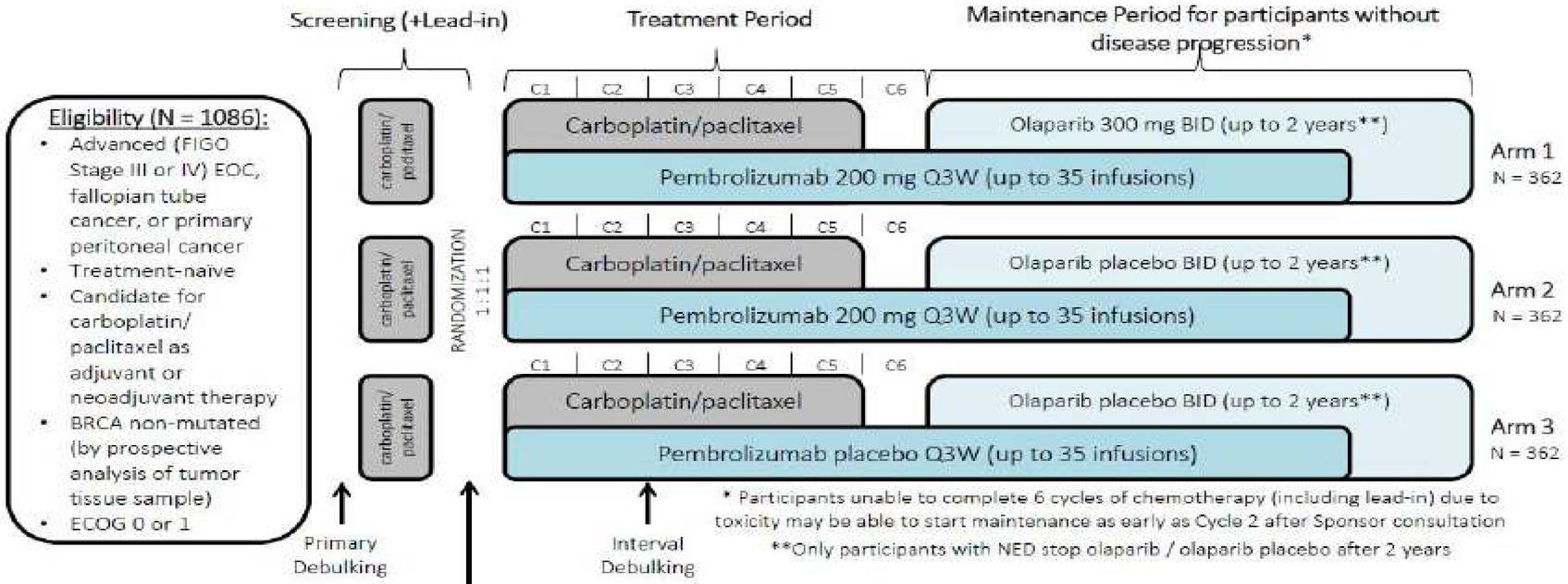
GOG-3036/KEYLYNK-001: MOA and Rationale

- Each of these modalities have at least some single agent activity in recurrent setting (g/t*BRCA*-wt)
- Each doublet has clinical activity in recurrent setting (g/t*BRCA*-wt)
  - PARPi/IOi (e.g., TOPACIO [niraparib/pembrolizumab])
  - PARPi/AAi (e.g., AVANOVA2 [niraparib/bevacizumab])
  - AAi/IO (e.g., bevacizumab/nivolumab)
- Extends some phase II/III findings in (g/t*BRCA*-wt) (GOG-0218, PRIMA, VELIA, MEDIOLA)



GOG-3036/KEYLYNK-001: Schema

N = 1086
Global Accrual: 1020
GOG Accrual = 70/200
GOG Activated Sites: 37/39
Primary Endpoint: PFS



Eligibility (N = 1086):

- Advanced (FIGO Stage III or IV) EOC, fallopian tube cancer, or primary peritoneal cancer
- Treatment-naïve
- Candidate for carboplatin/ paclitaxel as adjuvant or neoadjuvant therapy
- BRCA non-mutated (by prospective analysis of tumor tissue sample)
- ECOG 0 or 1

Stratify by:

- Surgery (planned interval debulking vs. R0 following primary debulking vs. R1 following primary debulking
- Bevacizumab use (yes vs. no)
- PD-L1 positivity (CPS <10 vs. CPS ≥10)

Investigator's Discretion:

Chemotherapy regimen

- Carboplatin AUC5 or AUC6 Q3W + Paclitaxel 175 mg/m^2 Q3W
- Carboplatin AUC5 or AUC6 Q3W + Paclitaxel 80 mg/m^2 QW
- Carboplatin AUC2 or AUC2.7 QW + Paclitaxel 60 mg/m^2 QW

Bevacizumab

- Administered per local standard of care and approved label
- For participants receiving adjuvant therapy, bevacizumab starts with Cycle 1
- For participants receiving neoadjuvant therapy, bevacizumab starts during lead-in, stops after Cycle 1, and resumes in Cycle 4
- If needed, bevacizumab may start as late as Cycle 4

GOG-3036/ KEYLYNK-001:

Key Eligibility Criteria

- Histologically confirmed FIGO Stage III or IV epithelial ovarian, primary peritoneal, or fallopian tube cancer;
- Has not received prior treatment for advanced or metastatic ovarian cancer;
- Eligible for primary or debulking surgery;
- Candidate for adjuvant or neoadjuvant carboplatin and paclitaxel chemotherapy;
- Able to provide a newly obtained core or excisional biopsy of a tumor lesion.
- BRCA non-mutated

Ovarian Platinum-Resistant

Ovarian

- Platinum-Resistant

  - **GOG-3029/INNOVATE-3**: Pivotal, Randomized, Open-label Study of Tumor Treating Fields (TTFields, 200kHz) Concomitant With Weekly Paclitaxel for the Treatment of Recurrent Ovarian Cancer (PI: David O'Malley, MD)

    ClinicalTrials.gov Identifier: NCT03940196

  - **GOG-3044/PROFECTA-II:** A Randomized Phase II, Open-Label, Multicenter, Parallel Two Arm Study of Afuresertib Plus Paclitaxel and Afuresertib Plus Carboplatin in Patients with Platinum-Resistant Ovarian Cancer (Thomas Herzog, MD)

    ClinicalTrials.gov Identifier: NCT04374630

  - **GOG-3045/MIRASOL**: A Randomized, Open-label, Phase 3 Study 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 (PI: Kathleen Moore, MD)

    ClinicalTrials.gov Identifier: NCT04209855

  - **GOG-3059**: A Phase 3, Randomized, Double-Blind, Adaptive, Placebo/Paclitaxel-Controlled Study of AVB-S6-500 in Combination with Paclitaxel in Patients with Platinum-Resistant Recurrent Ovarian Cancer (Katherine Fuh, MD, PhD)

GOG-3029/INNOVATE-3

Pivotal, Randomized, Open-Label Study of Tumor Treating Fields Concomitant with Weekly Paclitaxel for the Treatment of Platinum-Resistant Ovarian Cancer

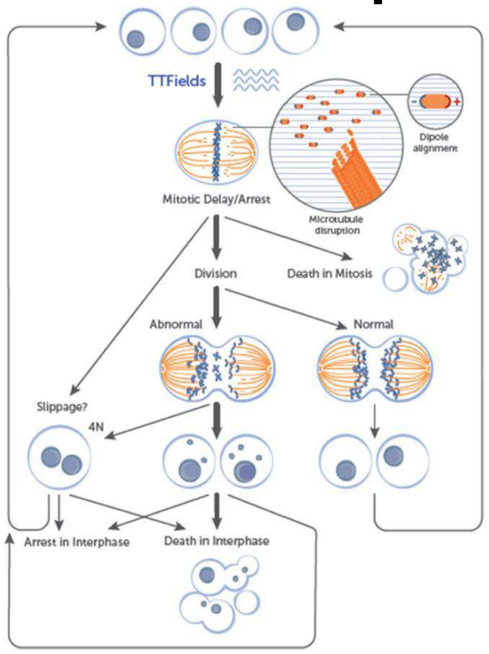
PI: David O'Malley, MD

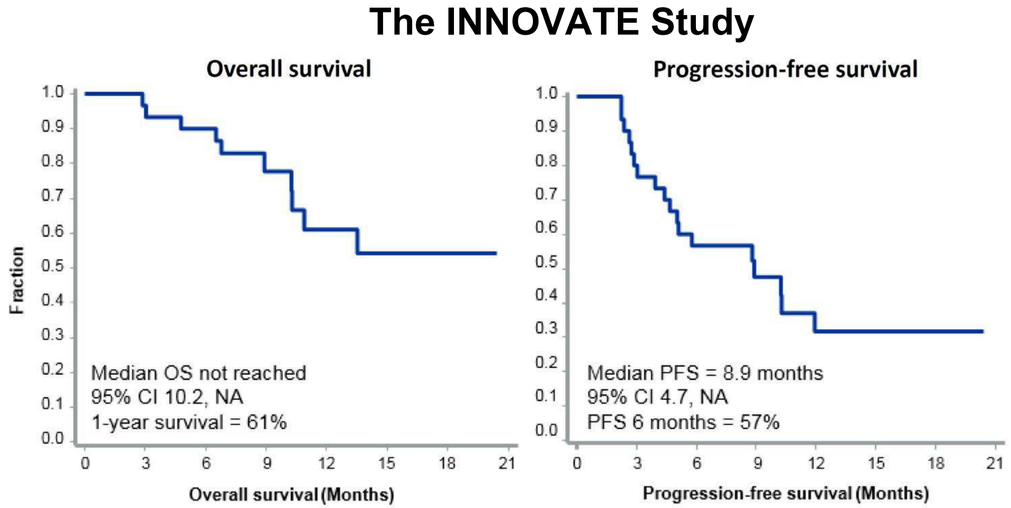
ClinicalTrials.gov Identifier: NCT03940196

GOG-3029/INNOVATE-3: MOA and Rationale

- Tumor Treating Fields (TTFields)
- FDA approvals in GBM in recurrent and primary therapy with standard chemotherapy
- Recent FDA approval in primary treatment of malignant pleural mesothelioma

- **Electric fields exert forces on charged tubulin proteins, disrupting formation of the mitotic spindle**



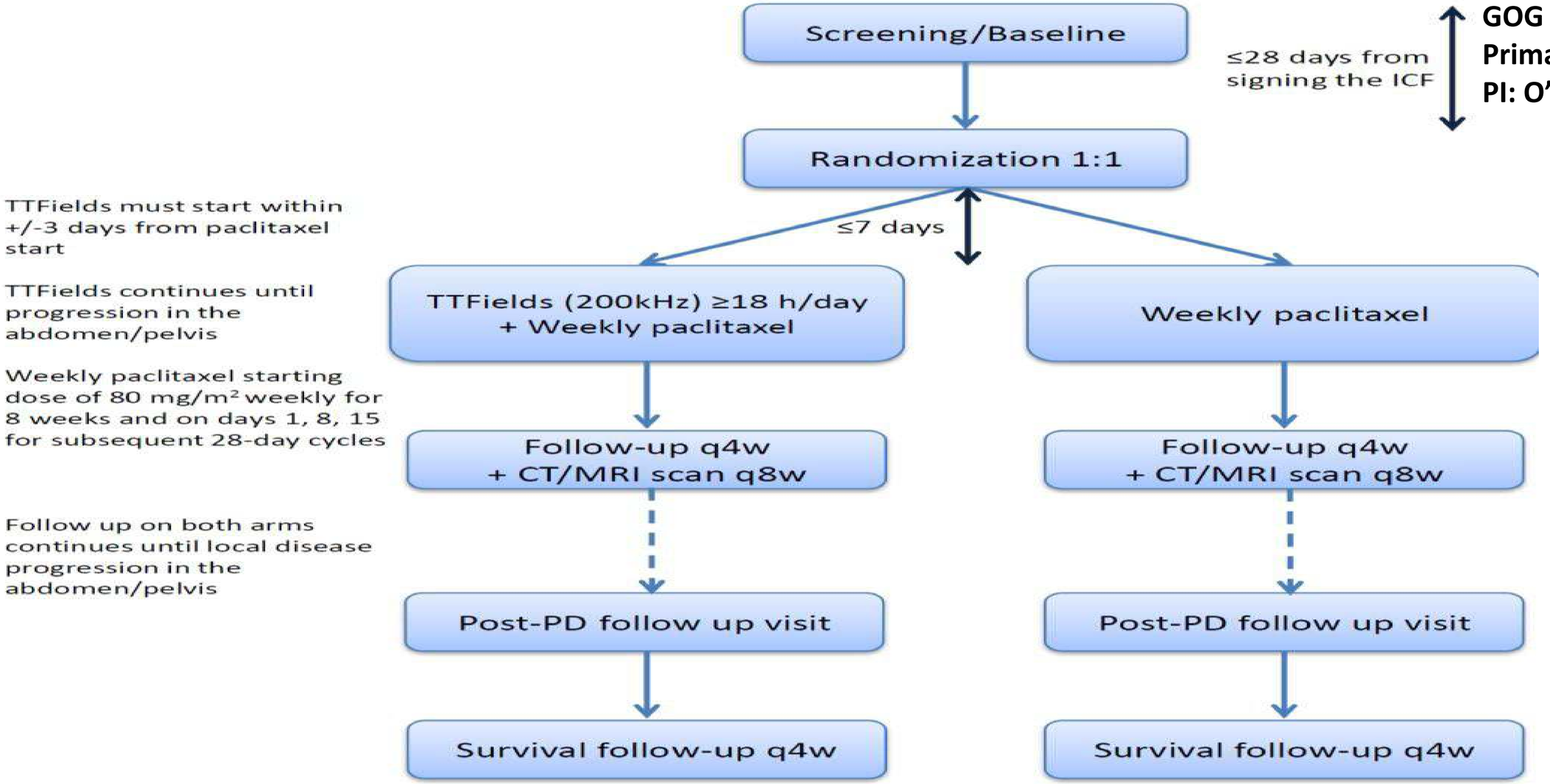


Vergote I., et al., *Gynecologic Oncology,* 2018; Giladi M., et al. *Scientific Reports*, 2015; Gera N, et al. *PLoS ONE*. 2015;10(5):e0125269. doi:10.1371/journal.pone.0125269.

GOG FOUNDATION

GOG-3029 INNOVATE-3: Schema

N = 540
Global Accrual: 305
GOG Accrual: 67/200
GOG Activated Sites: 41/46
Primary Endpoint: OS
PI: O'Malley



GOG FOUNDATION®

GOG-3029/ INNOVATE-3:

Key Eligibility Criteria

- Epithelial histology of ovarian/primary peritoneal or fallopian tube carcinoma at the time of diagnosis;
- Maximum two prior lines of systemic therapy following diagnosis of platinum-resistance;
- Maximum total of 5 prior lines of systemic therapy;
- Amenable to receive weekly paclitaxel and able to operate the NovoTTF-100L(O) System;
- ECOG 0-1;
- Evaluable (measurable or non-measurable) disease in the abdominal/pelvic region per RECIST v1.

GOG-3044/PROFECTA-II

An Open Label Randomized Active Controlled Phase II Clinical Study to Assess the Efficacy and Safety of Afuresertib Plus Paclitaxel Versus Paclitaxel in Patients With Platinum-Resistant Ovarian Cancer

PI: Tom Herzog, MD

ClinicalTrials.gov Identifier: NCT04374630

GOG-3044/PROFECTA-II: MOA and Rationale

- **Afuresertib**- MOA is a Pan AKT inhibitor
- Inhibits Akt 1/2/3
- AKT inhibition thought to restore chemo sensitivity
- Platinum resistant disease is a rational therapeutic target
- Can be combined with chemotherapy backbone
  - Phase IB data with paclitaxel and plat + paclitaxel

GOG-3044/PROFECTA-II: Schema (ver. 4.0)

-141 PROC Patients With 2:1 Ratio Randomization

N = 141
Global Accrual: 0
GOG Accrual: 2/102
GOG Activated Sites: 9/25
Primary Endpoint: PFS
PI: Herzog, T

PROC pts with:

- **Bev ineligible or PD;**
- **PARPi ineligible or PD;**
- **Failed prior 1 to 3 chemotherapies including no more than one chemo after PROC is diagnosed.**

D = Day; EOT = End of treatment; f/u = Follow-up; OS = Overall survival; PARPi = Poly ADP ribose polymerase inhibitor; PD: Progressive disease; PO = Per os (oral); PROC = Platinum-resistant ovarian cancer; Q3W = Once every 3 weeks; QD = Once daily.
EOT visit and safety follow-up: within 30 days (± 7 days) of last dose.
OS follow-up: every 12 weeks (± 7 days) continuing after EOT.
The afuresertib plus paclitaxel combination therapy arm starts from the first day (Day 1) after randomization. The PK study will be performed in both the afuresertib plus paclitaxel arm and paclitaxel alone arm.

GOG-3044/ PROFECTA-II:

Key Eligibility Criteria

- Must provide informed consent for the procedures & tests for PI3K/AKT/PTEN pathway alterations, BRCA1/2 mutations, and/or level of phospho-AKT. The archival tumor biopsy sample collected less than 1 year is preferred. If no archival tumor sample is available, fresh biopsy is recommended.
- Patients must have histologically or cytologically confirmed high grade serous OC, endometroid OC, or ovarian clear cell carcinoma (including fallopian tube and primary peritoneal cancers). Carcinosarcoma, sarcoma, mucinous OC, or low-grade serous histologies are excluded.
- Must not have previously received prior AKT or PI3K pathway or mTOR inhibitors.
- Must have PROC (including fallopian tube and primary peritoneal carcinoma), defined as cancer progression between 1 month and 6 months after completion of prior platinum-based therapy (at least 4 cycles). Progression is defined by RECIST 1.1 criteria in association with symptoms necessitating treatment.
- Must have received 1 to 3 prior chemotherapies including no more than one chemotherapy after PROC was diagnosed. No other additional anticancer treatment is allowed except for PARP inhibitor or bevacizumab. Combination therapy will be considered as one treatment, whereas maintenance therapy will be considered as continuation of the previous systemic treatment. Patients should be appropriate candidates for treatment with single agent weekly paclitaxel based on investigator's clinical assessment.
- Patients must either have received prior treatments with bevacizumab followed by disease progression, or bevacizumab cannot be used because of a specific contraindication

GOG-3045/MIRASOL

A Randomized, Open-label, Phase 3 Study 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

PI: Kathleen Moore, MD

ClinicalTrials.gov Identifier: NCT04209855

MIRASOL STUDY DESIGN
PHASE 3 REGISTRATION TRIAL FOR MIRVETUXIMAB USING PS2+ SCORING IN FRα HIGH PATIENTS

MIRASOL

ENROLLMENT AND KEY ELIGIBILITY

- 430 patients/330 events for PFS by INV
- FRα-high by PS2+ scoring
- Platinum resistant disease (<6 months PFI)
- Prior Bev and PARP allowed
- BRCAmut patients allowed

† PLD: pegylated liposomal doxorubicin
*BICR: Blinded Independent Central Review

N = 430
GOG Accrual: 26/200
GOG Activated Sites: 69/75
PI: Moore, K

1:1 RANDOMIZATION

Mirvetuximab Soravtansine

STRATIFICATION FACTORS
IC Chemotherapy Choice (Paclitaxel, PLD, Topotecan)
Prior Therapies (1 vs 2 vs 3)

Investigator's Choice Chemotherapy Paclitaxel, PLD†, or Topotecan

PRIMARY ENDPOINT
PFS by INV; BICR* for sensitivity analysis

SECONDARY ENDPOINTS
ORR by INV, OS, and PRO

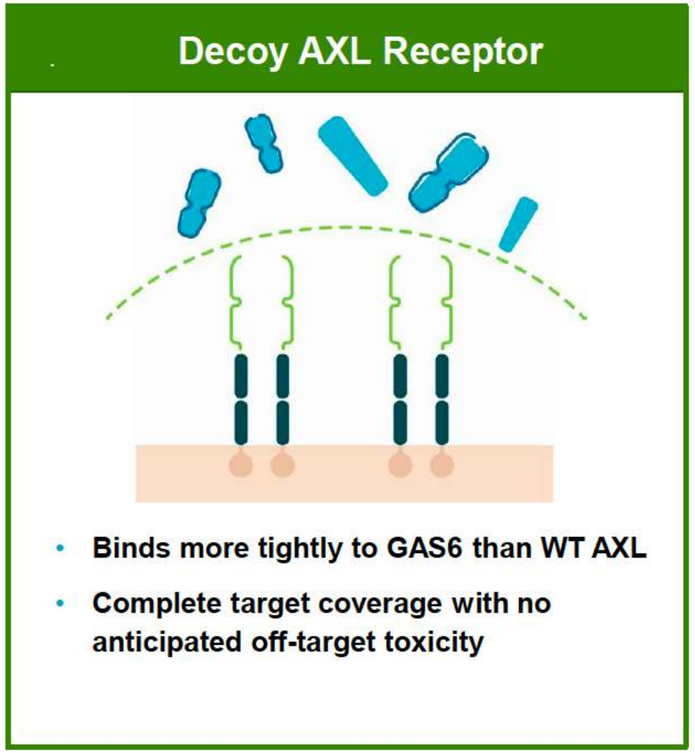
GOG-3059

A Phase 3, Randomized, Double-Blind, Adaptive, Placebo/Paclitaxel-Controlled Study of AVB-S6-500 in Combination with Paclitaxel in Patients with Platinum-Resistant Recurrent Ovarian Cancer

PI: Katherine Fuh, MD, PhD

GOG-3059/AVB500-OC-004

- Upcoming Phase III, double blind randomized trial comparing AVB-500 + Paclitaxel vs. Placebo + weekly paclitaxel sponsored by Aravive
- AVB-500 is high-affinity AXL decoy receptor that binds to GAS6, the sole ligand of AXL
- AXL is highly expressed in metastatic and advanced stage tumors in ovarian cancer
- Phase IB data demonstrated little to no added side effects of AVB-500 to paclitaxel
- Serum based biomarker will be used to correlate response to targeted agent
- GOG and study sponsor are looking for approximately 70 US sites.
- First site activated and patient randomized to be targeted for February 2021.



GOG-3059/AVB500-OC-004 :

Key Eligibility Criteria

- Histologically confirmed and documented recurrent ovarian, fallopian tube or peritoneal cancer. Only patients with high-grade serous adenocarcinoma histology are eligible;
- Prior treatment with one to four prior therapy regimens;
- Platinum-resistant disease (disease progression within 6 months of last platinum therapy);
- ECOG 0-1;
- Prior bevacizumab is allowed.

If interested in participating, please contact Katie Campbell at kcampbell@gog.org

Platinum Resistant Ovarian Cancer (PROC)

Comparison of PROC Trials

	GOG-3018 (OVAL)	GOG-3029 (INNOVATE-3)	GOG-3032 (MOONSTONE)	GOG-3044 (PROFECTA)	GOG-3045 (MIRASOL)	GOG-3048 (Mersana)	GOG-3059 (Aravive)	NRG-GY009
Phase	3	3	2	2	3	1b	3	2/3
Regimen	VB-111/placebo D1 (56 day cycle) + weekly paclitaxel vs. weekly Paclitaxel	TTFields >18 hr/day + weekly paclitaxel vs. weekly Paclitaxel	Niraparib daily + Dostarlimab D1 (3-week cycle)	Afuresertib PO QD + Paclitaxel D1,8,15 Q3W vs. weekly Paclitaxel	Mirvetuximab vs Investigator Choice chemotherapy	XMT-1536 every 4 weeks	AVB-S6-500 (D1 & 15) + Weekly paclitaxel (D 1, 8, 15 on a 28d cycle) vs. weekly Paclitaxel	PLD/Atezo (D1&15) vs. PLD/Bev(D1&15)/ Atezo (D1&15) vs. PLD/Bev (D1&15)
Prior total therapies	≤ 5	≤ 5	1-3	1-3 prior platinum	1-3	1-3 (permission can be granted for 4 prior)	1-4	1-2
Prior therapies for PROC	< 3	< 3	1-2	0	not defined	not defined (only 2 prior taxanes allowed)	not defined (no prior taxanes for recurrence)	not defined
Tumor Testing/Prevalence	No	No	yes	yes	yes	no	no	no

Comparison of PROC Trials

	GOG-3018 (OVAL)	GOG-3029 (INNOVATE-3)	GOG-3032 (MOONSTONE)	GOG-3044 (PROFECTA)	GOG-3045 (MIRASOL)	GOG-3048 (Mersana)	GOG-3059 (Aravive)	NRG-GY009
Phase	3	3	2	2	3	1b	3	2/3
Regimen	VB-111/placebo D1 (56 day cycle) + weekly paclitaxel vs. weekly Paclitaxel	TTFields >18 hr/day + weekly paclitaxel vs. weekly Paclitaxel	Niraparib daily + Dostarlimab D1 (3-week cycle)	Afuresertib PO QD + Paclitaxel D1,8,15 Q3W vs. weekly Paclitaxel	Mirvetuximab vs Investigator Choice chemotherapy	XMT-1536 every 4 weeks	AVB-S6-500 (D1 & 15) + Weekly paclitaxel (D 1, 8, 15 on a 28d cycle) vs. weekly Paclitaxel	PLD/Atezo (D1&15) vs. PLD/Bev(D1&15)/ Atezo (D1&15) vs. PLD/Bev (D1&15)
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Tumor Testing/Prevalence	No	No	yes	yes	yes	no	no	no

Comparison of PROC Trials

	GOG-3018 (OVAL)	GOG-3029 (INNOVATE-3)	GOG-3032 (MOONSTONE)	GOG-3044 (PROFECTA)	GOG-3045 (MIRASOL)	GOG-3048 (Mersana)	GOG-3059 (Aravive)	NRG-GY009
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Tumor Testing/Prevalence	No	No	yes	yes	yes	no	no	no

Comparison of PROC Trials

	GOG-3018 (OVAL)	GOG-3029 (INNOVATE-3)	GOG-3032 (MOONSTONE)	GOG-3044 (PROFECTA)	GOG-3045 (MIRASOL)	GOG-3048 (Mersana)	GOG-3059 (Aravive)	NRG-GY009
Phase	3	3	2	2	3	1b	3	2/3
Regimen	VB-111/placebo D1 (56 day cycle) + weekly paclitaxel vs. weekly Paclitaxel	TTFields >18 hr/day + weekly paclitaxel vs. weekly Paclitaxel	Niraparib daily + Dostarlimab D1 (3-week cycle)	Afuresertib PO QD + Paclitaxel D1,8,15 Q3W vs. weekly Paclitaxel	Mirvetuximab vs Investigator Choice chemotherapy	XMT-1536 every 4 weeks	AVB-S6-500 (D1 & 15) + Weekly paclitaxel (D 1, 8, 15 on a 28d cycle) vs. weekly Paclitaxel	PLD/Atezo (D1&15) vs. PLD/Bev(D1&15)/ Atezo (D1&15) vs. PLD/Bev (D1&15)
Prior total therapies	≤ 5	≤ 5	1-3	1-3 prior platinum	1-3	1-3 (permission can be granted for 4 prior)	1-4	1-2
Prior therapies for PROC	< 3	< 3	1-2	0	not defined	not defined (only 2 prior taxanes allowed)	not defined (no prior taxanes for recurrence)	not defined
Tumor Testing/Prevalence	No	No	yes	yes	yes	no	no	no

Comparison of PROC Trials

	GOG-3018 (OVAL)	GOG-3029 (INNOVATE-3)	GOG-3032 (MOONSTONE)	GOG-3044 (PROFECTA)	GOG-3045 (MIRASOL)	GOG-3048 (Mersana)	GOG-3059 (Aravive)	NRG-GY009
Definition of Platinum-Resistance	1. CT confirmed progression disease within 90 - 180 days from completion of a minimum of 4 platinum therapy OR 2. Platinum-refractory disease defined as CT confirmed progression during platinum therapy or up to 90 days from the last platinum.	Progression < 6 months from completion of a minimum of four cycles of platinum (as evidenced by radiographic progression per RECIST v.1.1)	Progression < 6 months from completion of a minimum of four cycles of platinum (as evidenced by radiographic progression per RECIST v.1.1)	1. Cancer progression 1-6m after platinum (at least 4 cycles). 2. Exclusion for Platinum-refractory disease (progression <1 m platinum)	Progression < 6 months from completion of a minimum of four cycles of platinum	Progression < 6 months from completion of a minimum of four cycles of platinum	Progression < 6 months from completion of platinum	Progression < 6 months from completion of platinum
Non-high grade serous/ endometrioid Histologies Allowed	no	no	yes (clear cell)	yes (clear cell)	No (endometrioid not allowed)	No (endometrioid not allowed)	No (endometrioid not allowed)	yes (clear cell; undiff, adenoCa NOS)
Frequency of Visits	weekly	weekly	every 3 weeks for 4 cycles, then every 6 weeks on cycle 5	3 times each cycle (cycle = 3 weeks)	MIRV every 3 weeks (cycle = 3 weeks)	every 4 weeks (cycle = 4 weeks)	Weekly (3 of 4 weeks)	day 1 and 15 of each 28-day period (cycle = 4 weeks)
Primary Platinum Refractory Allowed (defined)	Yes (<90 days)	No (1 month)	No (<3 months)	No (<1 month)	No (<3 months)	No (<3 months)	No (<1 month)	No (not defined)

The OSU/James Schema for PROC

Platinum Resistant Ovarian, Primary Peritoneal, & Tubal Cancer

Updated 12.21.2020

Measurable Or Non-Measurable

Measurable

1st PD 2nd Line Persistent Disease	**NRG-GY009 (Ph3)** Lead: Callan Myerscough Doxil/Atezo/Bev High grade epithelial: **Excluded:** LGS, mucinous, MMMT; prior checkpoint/PLD; prior Bev for plat resistance	**OSU-18199/NCI 10150 (Ph2)** Lead: Callan Myerscough Bev + Wkly Taxol or Wkly anetumab ravtansine; MSLN positive tumor required; **Excluded:** No LGS, sarcoma	**OSU-20092 / Clovis (Ph2)** Lead: Delrina Crump Ovarian Clear Cell Lucitinib & Nivo **Excluded:** Prior check point or VEGF-TKI (prior Bev only allowed first line)	**OSU-18027 (Ph1)** Lead: Ridge Archer **REGN4018 +/- Cemiplimab** Must have elevated CA-125; No standard options/platinum intolerant; No MMMT Waitlist only								
1st PD 2nd Line < 6 months	**OSU-18007 (Exp)** Lead: Kelly Dodd IMGN853 & Rucaparib Folate positive tumor No LGS or clear cell unless gBRCA+; Can't be primary plat refractory (<3 month PFI)	**NRG-GY009 (Ph3)** Lead: Callan Myerscough Doxil/Atezo/Bev High grade epithelial: **Excluded:** LGS, mucinous, MMMT; prior checkpoint/ PLD; prior Bev for plat resistance	**OSU-18199/NCI 10150 (Ph2)** Lead: Callan Myerscough Bev + Wkly Taxol or Wkly anetumab ravtansine; MSLN positive tumor **Excluded:** LGS, sarcoma;	**OSU-20015 (Ph3)** Lead: Jill Kent Weekly Taxol + TTFields Epithelial types; Only 2 prior lines for plat resistance; **Excluded** if PD </= 1 months first platinum	**OSU-20214 (Ph3)** Mirvetuximab Sora vs MD Choice Chemo Lead: Callan Myerscough High grade serous only FRα positive **Excluded:** First line PFI < 3 months; see eye disorders	**OSU-20092 / Clovis** Lead: Delrina Crump Ovarian Clear Cell Lucitinib & Nivo **Excluded:** Prior check point or VEGF-TKI (prior Bev only allowed first line)	**OSU-16293 (GSK)** Lead: Anna Brantley **TRS-042 / Cohort G** High grade epithelial types **Excluded:** prior checkpoint; PD within 3 months first platinum; Known sBRCA or gBRCA	**OSU-18220 (Ph2)** Part B Lead: Sarah Hwang Tisotumab Vedotin Prior Bev required; **Excluded:** MMMT, LGS, or mucinous; PFI to first line </= 3 months	**OSU-18027 (Ph1)** Lead: Ridge Archer **REGN4018 +/- Cemiplimab** Must have elevated CA-125; No standard/plat intolerant; No MMMT Waitlist only	**SWOG-S1609** **Ipi & Nivo; Cohort 49/ 50** Lead: Kelly Dodd PD-L1 amplified tumors or small cell (hypercalcemic) No standard tx available	
2nd PD 3rd Line	**OSU-18007 (Exp)** Lead: Kelly Dodd IMGN853 & Rucaparib Folate positive tumor No LGS or clear cell unless gBRCA+; Can't be primary plat refractory (<3 month PFI)	**NRG-GY009 (Ph3)** Lead: Callan Myerscough Doxil/Atezo/Bev High grade epithelial: **Excluded:** LGS, mucinous, MMMT; prior checkpoint/ PLD; prior Bev for plat resistance	**OSU-18199/NCI 10150 (Ph2)** Lead: Callan Myerscough Bev + Wkly Taxol or Wkly anetumab ravtansine; MSLN positive tumor **Excluded:** LGS, sarcoma;	**OSU-20015 (Ph3)** Lead: Jill Kent Weekly Taxol + TTFields Epithelial types; Only 2 prior lines for plat resistance; **Excluded** if PD </= 1 months first platinum	**OSU-20214 (Ph3)** Mirvetuximab Sora vs MD Choice Chemo Lead: Callan Myerscough High grade serous only FRα positive **Excluded:** First line PFI < 3 months; see eye disorders	**OSU-19094 (Ph1) – Exp** Lead: Anyssa Armstead **Mersana / XMT-1536** Tumor Expresses NaPi2b; HGS; No PD within 6 months of first/primary tx	**OSU-18220 (Ph2)** Part B Lead: Sarah Hwang Tisotumab Vedotin Prior Bev required; **Excluded:** MMMT, LGS, or mucinous; PFI to first line </ = 3 months	**OSU-20092** Lead: Delrina Crump Ovarian Clear Cell Cohort Lucitinib & Nivo **Excluded:** Prior check point or VEGF-TKI (prior Bev only allowed first line)	**OSU-16293 (GSK)** Lead: Anna Brantley **TRS-042 / Cohort G** High grade epithelial types **Excluded:** prior checkpoint; PD within 3 months first platinum; Known sBRCA or gBRCA	**OSU-18027 (Ph1)** Lead: Ridge Archer **REGN4018 +/- Cemiplimab** Must have elevated CA-125; No standard/plat intolerant; No MMMT Waitlist only	**SWOG-S1609** **Ipi & Nivo; Cohort 49/ 50** Lead: Kelly Dodd PD-L1 amplified tumors or small cell (hypercalcemic) No standard tx available
3rd PD 4th Line	**OSU-18007 (Exp)** Lead: Kelly Dodd IMGN853 & Rucaparib Folate positive tumor No LGS or clear cell unless gBRCA+; Can't be primary plat refractory (<3 month PFI)	**OSU-20015 (Ph3)** Lead: Jill Kent Weekly Taxol + TTFields Epithelial types; Only 2 prior lines for plat resistance; **Excluded** if PD </= 1 months first platinum	**OSU-18199/NCI 10150 (Ph2)** Lead: Callan Myerscough Bev + Wkly Taxol or Wkly anetumab ravtansine; MSLN positive tumor **Excluded:** LGS, sarcoma;	**OSU-18220 (Ph2)** Part B Lead: Sarah Hwang Tisotumab Vedotin Prior Bev required; **Excluded:** MMMT, LGS, or mucinous; PFI to first line </= 3 months	**OSU-20214 (Ph3)** Mirvetuximab Sora vs MD Choice Chemo Lead: Callan Myerscough High grade serous only FRα positive **Excluded:** First line PFI < 3 months; see eye disorders	**OSU-19094 (Ph1) – Exp** Lead: Anyssa Armstead **Mersana / XMT-1536** Tumor testing NaPi2b; HGS only; No PD within 6 months of first/ primary tx	**OSU-20092** Lead: Delrina Crump Ovarian Clear Cell Cohort Lucitinib & Nivo **Excluded:** Prior check point or VEGF-TKI (prior Bev only allowed first line)	**OSU-16293 (GSK)** Lead: Anna Brantley **TRS-042 / Cohort G** High grade epithelial types **Excluded:** prior checkpoint; PD within 3 months first platinum; Known sBRCA or gBRCA	**OSU-18027 (Ph1)** Lead: Ridge Archer **REGN4018 +/- Cemiplimab** Must have elevated CA-125; No standard/plat intolerant; No MMMT Waitlist only	**SWOG-S1609** **Ipi & Nivo; Cohort 49/50** Lead: Kelly Dodd PD-L1 amplified tumors or small cell (hypercalcemic) No standard tx available	
4th PD 5th Line	**OSU-18007 (Exp)** Lead: Kelly Dodd IMGN853 & Rucaparib Folate positive tumor No LGS or clear cell unless gBRCA+; Can't be primary plat refractory (<3 month PFI)	**OSU-20015 (Ph3)** Lead: Jill Kent Weekly Taxol + TTFields Epithelial types; Only 2 prior lines for plat resistance; **Excluded** if PD </= 1 months first platinum	**OSU-18199/NCI 10150 (Ph2)** Lead: Callan Myerscough Bev + Wkly Taxol or Wkly anetumab ravtansine; MSLN positive tumor **Excluded:** LGS, sarcoma;	**OSU-20092** Lead: Delrina Crump Ovarian Clear Cell Cohort Lucitinib & Nivo **Excluded:** Prior check point or VEGF-TKI (prior Bev only allowed first line)	**OSU-18027 (Ph1)** Lead: Ridge Archer **REGN4018 +/- Cemiplimab** Must have elevated CA-125; No standard/plat intolerant; No MMMT Waitlist only	**SWOG-S1609** **Ipi & Nivo; Cohort 49/ 50** Lead: Kelly Dodd PD-L1 amplified tumors or small cell (hypercalcemic) No standard tx available					
6+ Lines	**OSU-18199/NCI 10150 (Ph2)** Lead: Callan Myerscough Bev + Wkly Taxol or Wkly anetumab ravtansine; MSLN positive tumor **Excluded:** LGS, sarcoma;	**OSU-20092** Lead: Delrina Crump Ovarian Clear Cell Cohort Lucitinib & Nivo **Excluded:** Prior check point or VEGF-TKI (prior Bev only allowed first line)	**OSU-18027 (Ph1)** Lead: Ridge Archer **REGN4018 +/- Cemiplimab** Must have elevated CA-125; No standard/plat intolerant; No MMMT Waitlist only	**SWOG-S1609** **Ipi & Nivo; Cohort 49/50** Lead: Kelly Dodd PD-L1 amplified tumors or small cell (hypercalcemic) No standard tx available								

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Can/Should I Open more than 1 PROC trial?

Case Studies

- A patient with primary platinum resistance (1 prior line):
  - First treatment: GY009 (PLD +/- Atezo +/- Bev)
  - Second Treatment: 3045 (MIRASOL) or 3048 (Mersana)
  - Third Treatment: 3032 (MOONSTONE) - if didn't receive Atezo with GY009
  - Fourth Line: weekly paclitaxel regimen
    - 3018 (OVAL)
    - 3029 (INNOVATE-3)
    - 3059 (Aravive) ****Important to consider the projected closure dates of the above trials*****

- A patient who has received 3 prior lines of therapy (2 platinum regimens and an additional regimen)
  - 4th Line (first PROC trial): 3045 (MIRASOL)
  - 5th Line (2nd PROC trial): weekly paclitaxel regimen (3018/OVAL; 3029/INNOVATE; 3059/Aravive)

Can/Should I Open more than 1 PROC trial? YES!!!!!!!!

- Alternative:
  - Weekly topo:
    - 0% ORR in AURELIA
    - 12% ORR weekly (146Q)
    - 27% ORR daily (146Q)
  - Single Agent PLD: 8% ORR in AURELIA
  - PLD: 4% ORR in JAVELIN 200
  - PLD/Bev: 14% ORR in AURELIA
  - PLD/Pac/Topo: 16% ORR in FORWARD-1
- Expectation:
  - Institutions should have 2-5 trials open for PROC
  - Prioritize clinical trials in this population

- PROC is arguably our greatest unmet need
- Consider institutional algorithms which help prioritize trials in a sequential fashion
- Tissue Testing prior to clear progression (screening consents)

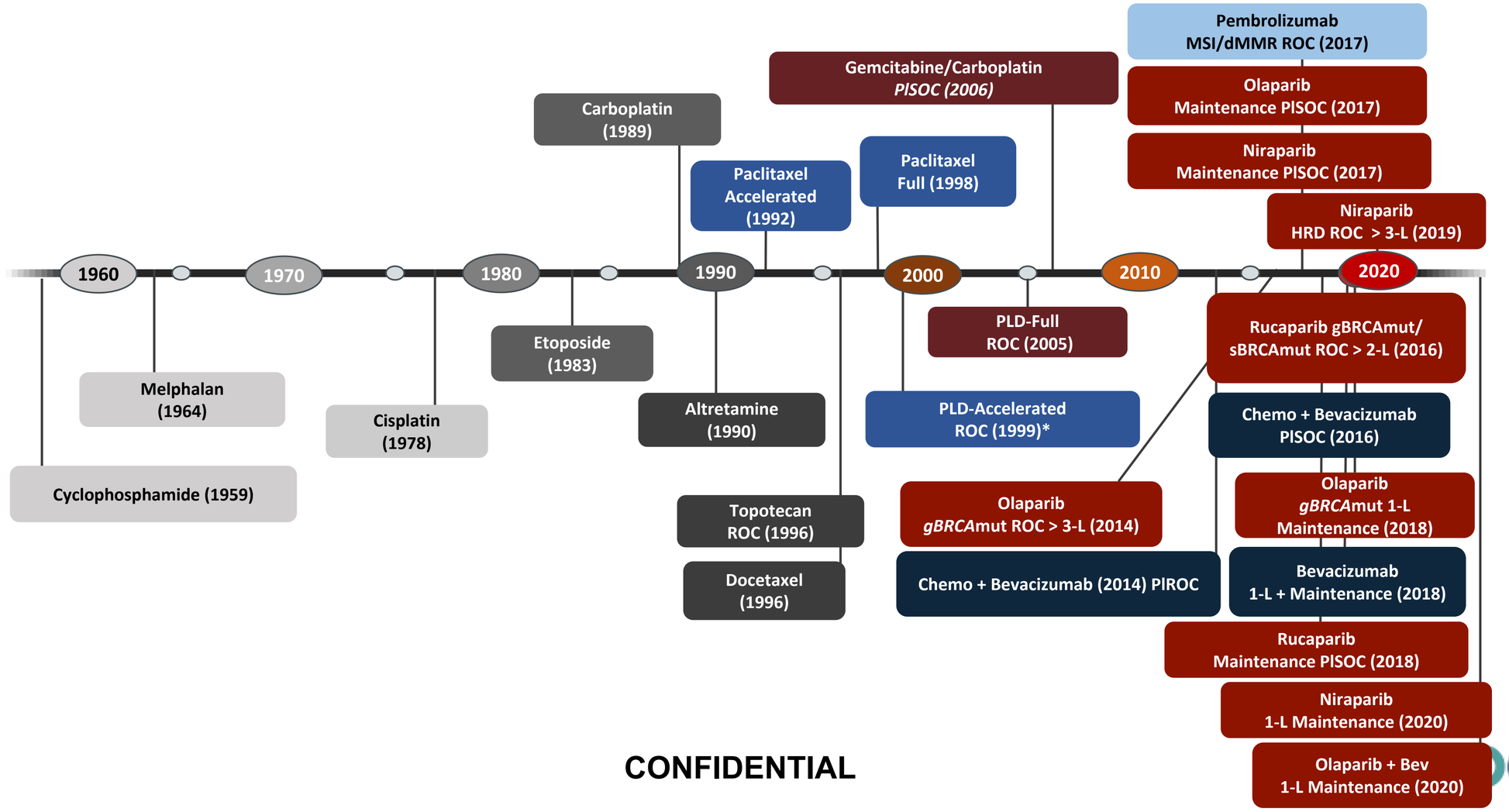
- GOG-P can help
  - Provide information which highlights the differences to prepare for IRB/SRCs reviews
  - Help predict when trials will be closing to help in defining the queue

Thomas J Herzog 1, Michael W Sill, Joan L Walker, David O'Malley, Mark Shahin, Koen DeGeest, Sheldon A Weiner, David Mutch, Robert L DeBernardo, Samuel S Lentz. Gynecol Oncol. 2011 Mar;120(3):454-8. doi: 10.1016/j.ygyno.2010.11.008. Epub 2010 Dec 17. A phase II study of two topotecan regimens evaluated in recurrent platinum-sensitive ovarian, fallopian tube or primary peritoneal cancer: a Gynecologic Oncology Group Study (GOG 146Q)

Moore K, Forward-1. ESMO 2019

FDA-Approved Drugs for Ovarian Cancer

12+ Approvals since Nov 2014
More approvals in the last 6 years than the prior 60 years combined



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Transforming the standard of care

Thank you

The James

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Creating a cancer-free world. One person, one discovery at a time.