Emerging Endometrial Trials

Brian Slomovitz, MD
Mount Sinai Medical Center, Miami Beach, FL

GOG FOUNDATION®
Transforming the standard of care

GOG Highlight Reel

GOG FOUNDATION®
Transforming the standard of care

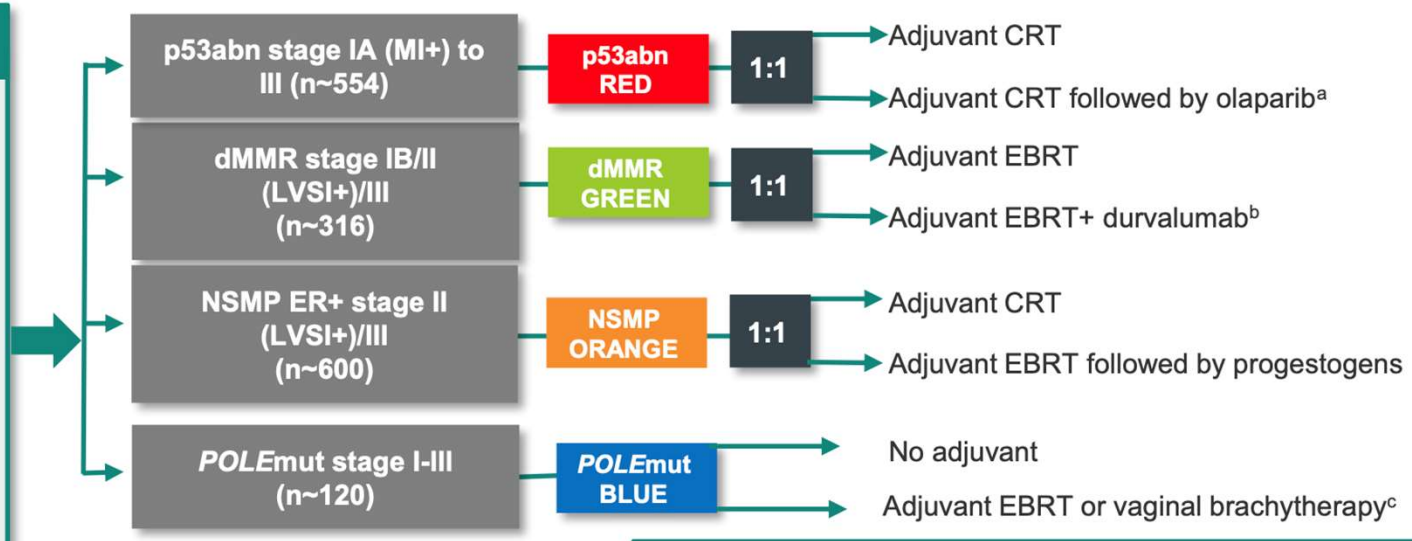
Adjuvant Trials

GOG Highlight Reel

NRG-GY032 RAINBO: Phase II/III Trials Investigating Adjuvant Therapy in Endometrial Cancer Based on Molecular Features

Patient Population (N≈1615)

- Hysterectomy and bilateral salpingo-oophorectomy ± lymphadenectomy or sentinel node biopsy, without residual disease after surgery
- Endometrioid, serous, clear cell, un/dedifferentiated, mixed, and carcinosarcoma cell types
- Full molecular classification performed according to the WHO 2020 diagnostic algorithm
- Expected start of adjuvant treatment (if applicable) within 10 weeks after surgery
- No distant metastases as determined by presurgical or postsurgical imaging (CT scan of chest, abdomen, and pelvis or whole-body PET-CT scan)



Primary Endpoints

- 3-year RFS (p53abn-RED, dMMR-GREEN, and NSMP-ORANGE trials)
- 3-year pelvic RFS (*POLE*mut-BLUE trial)

Secondary Endpoints

- 5-year RFS (overall, pelvic)
- 3- and 5-year vaginal RFS
- 3- and 5-year survival (overall and EC-specific)
- Safety and HRQoL

[a]Olaparib and progestogens ≤ 2 years after adjuvant RT. [b]Durvalumab for 1 year total (during and after adjuvant RT). [c]The *POLE*mut-BLUE trial will recruit 120 patients with select stage I–II *POLE*mut endometrial cancer in the main "lower risk" study cohort.
WHO = World Health Organization; CT = computed tomography; PET-CT = positron emission tomography-CT; LVSI = lymphovascular space invasion; MI = microsatellite instability; HRQoL = health-related quality of life.
ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated July 13, 2023. Accessed April 10, 2024.
https://clinicaltrials.gov/study/NCT05255653. RAINBO Research Consortium. *Int J Gynecol Cancer*. 2022;33(1):109-117.

Unmet Needs…

ENGOT-en11/GOG-3053/KEYNOTE-B21 Replacement

Is it possible to do another adjuvant trial?

GOG FOUNDATION®
Transforming the standard of care™

GOG Highlight Reel

GOG FOUNDATION®
Transforming the standard of care

First-Line Trials

GOG Highlight Reel

NRG GY-026

Newly Diagnosed, Stage I-IVB, HER2 positive uterine serous or carcinosarcoma

Randomize 1:1:1

PI: Britt Erickson
Co-PI: Amanda Fader
Intl Co-PI: Clare Scott
TransIx PI: Alessandro Santin

Safety Lead-In (n=45)

Arm 1: Carboplatin AUC 5 + paclitaxel 175 mg/m2 q 21 days x 6 cycles (may continue to 10 cycles if measurable disease and SD or PR)

Arm 2: Carboplatin AUC 5 + paclitaxel 175 mg/m2 q 21 days x 6 cycles + trastuzumab 8 mg/kg IV loading dose f/b 6 mg/kg IV q 21 days

Arm 3: Carboplatin AUC 5 + paclitaxel 175 mg/m2 q 21 days x 6 cycles + fixed dose trastuzumab 600 mg/ pertuzumab 600 mg SQ (with initial 1200 mg SQ pertuzumab loading dose w 1st cycle)

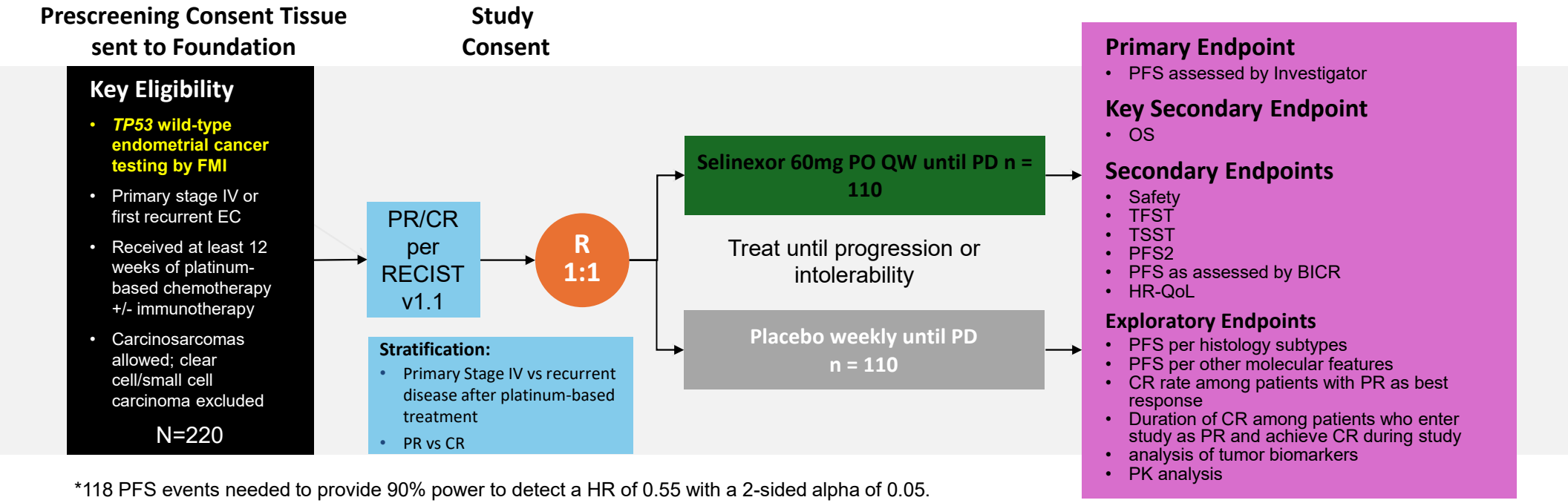
Strata:
- **Stage (I-II vs III-IV)**
- **Measurable vs. non-measurable dz**
- **Histology (serous vs carcinosarcoma)**

Maintenance trastuzumab 6mg/kg IV every 21 days x 1 year (or progression/ prohibitive toxicity)

Maintenance fixed dose trastuzumab 600 mg/ pertuzumab 600 mg SQ q 21 days for 1 year (or until disease progression or prohibitive toxicity)

NCT05256225

XPORT-EC-042/GOG-3083: A Phase 3, Randomized, Placebo-Controlled, Double-Blind, Multicenter Trial of Selinexor in Maintenance Therapy After Systemic Therapy for Patients With *TP53* Wild-type, Advanced, or Recurrent EC



*118 PFS events needed to provide 90% power to detect a HR of 0.55 with a 2-sided alpha of 0.05.

NCT05611931

EC, endometrial cancer; FMI, Foundation Medicine; BICR, blinded independent central review; CR, complete response; DCR, disease control rate; EC, endometrial cancer; HR-QoL, health-related quality of life; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; PFS2, time from randomization until the second progression event; PD, progressive disease; PK, pharmacokinetics; PR, partial response; R, randomized; RECIST, Response Evaluation Criterial in Solid Tumors; TFST, time to first subsequent treatment; TSST, time to second subsequent treatment; QW, every week.

Unmet Needs…

Move ADCs to first-line?

First-line biomarker/hormonal trial?

Is a first-line hormonal therapy versus SOC trial feasible in the right patient population?

Continue to explore role of IO in first-line for pMMR tumors?

GOG FOUNDATION®
Transforming the standard of care™

GOG Highlight Reel

GOG FOUNDATION®
Transforming the standard of care

Second-Line and Beyond Trials

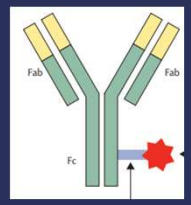
GOG Highlight Reel

GOG FOUNDATION®
Transforming the standard of care

ADCs Under Development

Target

- HER2
- TROP2
- B7H4
- Alpha-Folate Receptor
- Others



GOG Highlight Reel

GOG FOUNDATION®
Transforming the standard of care

Second Line, Phase 3 Trials – ADC

GOG-3095/MK-2870-005/ENGOT-en23: ***A Phase 3, Randomized, Active-controlled, Open-label, Multicenter Study to Compare the Efficacy and Safety of MK-2870 Monotherapy Versus Treatment of Physician's Choice in Participants With Endometrial Cancer Who Have Received Prior Platinum-based Chemotherapy and Immunotherapy (PI: Bhavana Pothuri, MD, Junior PI: Michelle Lightfoot, MD)*** **NCT06132958**

ASCENT-GYN-01/GOG-3104/ENGOT-en26: ***A Randomized, Open-Label, Phase 3 Study of SG vs TPC in Participants With Endometrial Cancer Who Have Received Prior Platinum-Based Chemotherapy and Anti-PD-1/PD-L1 Immunotherapy (PI: Ramez Eskander, MD, Co-PI: Bradley Corr, MD)*** **NCT06486441**

GOG Highlight Reel

Non- ADCs in Development in EC

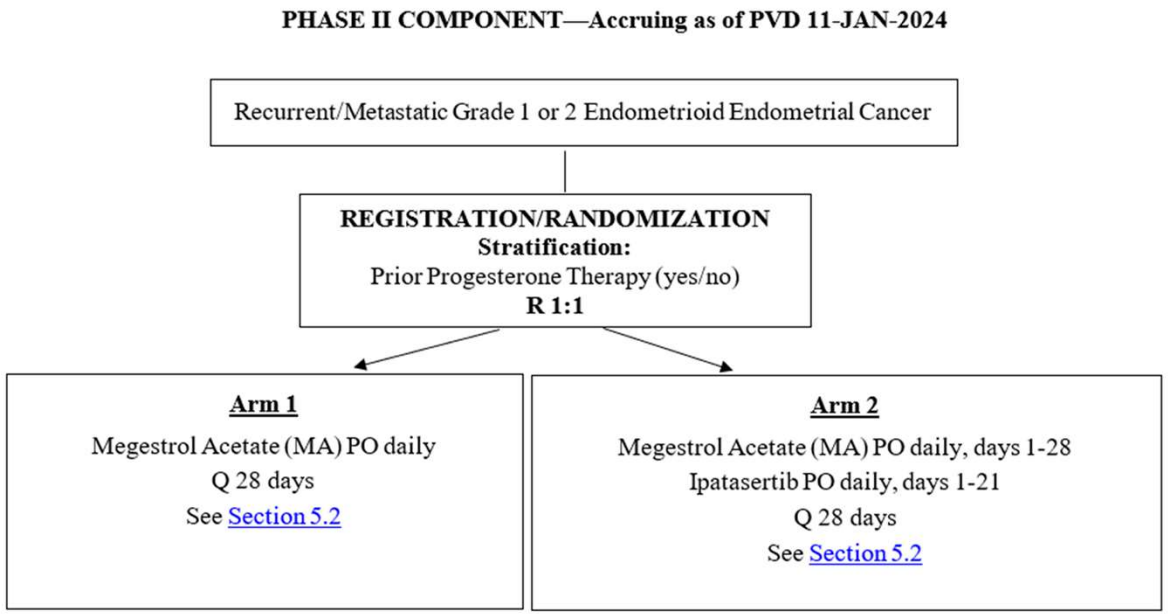
Sponsor	Agent	Target/MOA	clinicaltrials.gov
Zentalis	Azenosertib	WEE1 inhibitor	NCT04814108 GOG-3065
Acrivon	ACR-368 (Prexasertib)	CHK1 and CHK2 inhibitor	NCT0554829* GOG-3082
Faeth	Serabelisib + Sapanisertib	PI3K/AKT/mT OR inhibitor	NCT06463028* GOG-3011

* Biomarker informed populations

NRG-GY028

A Phase IB and Randomized Phase II Trial of Medroxyprogesterone Acetate with or without Ipatasertib in Recurrent or Metastatic Endometrioid Endometrial Cancer

PI: Michaela Onstad | Co-PI: Shannon Westin, MD



- Phase IB = Complete
- Phase II = 78

Primary endpoint:
- Phase IB: Safety
- Phase II: PFS

NCT05538897

GOG Highlight Reel

GOG FOUNDATION

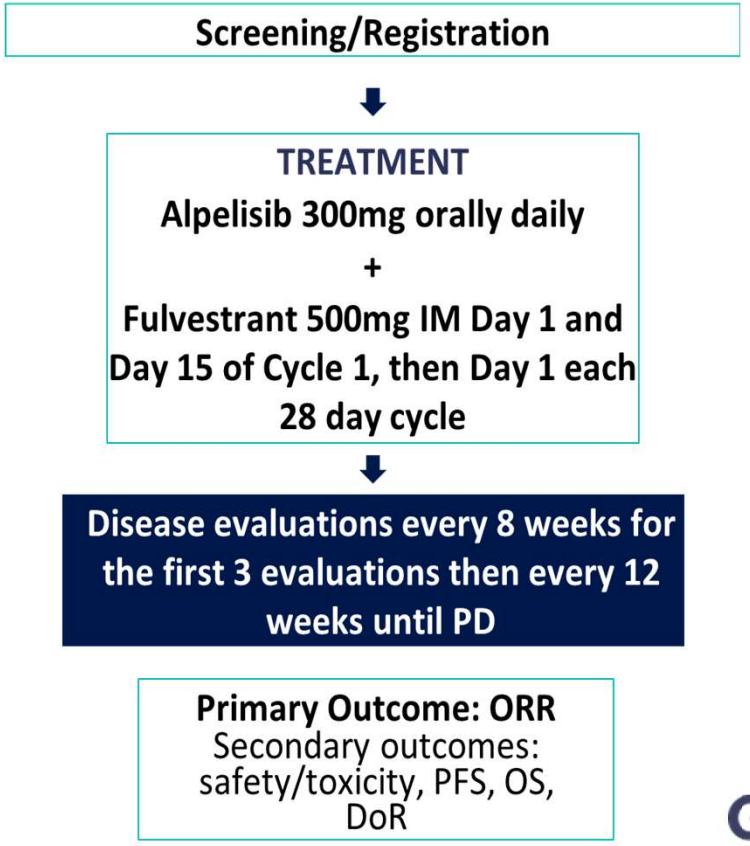
GOG-3069

A Phase 2 Study of Alpelisib and Fulvestrant for PIK3CA-mutated Estrogen Receptor (ER) Positive Endometroid Endometrial Cancer

PI: Stephanie Gaillard, MD | Co-PI: Brian Slomovitz, MD

Key Eligibility:

- Advanced, persistent, recurrent endometrial cancer
  - Endometroid histology
  - PIK3CA mutated (CLIA-certified testing)*
  - ER+ (greater than or equal to 1% of tumor cells)
- Measurable disease by RECIST v1.1
- Prior endocrine therapy allowed
- No prior mTOR, PIK3CA, PI3K, or AKT inhibitors allowed



SCAN ME

NCT05154487

Unmet Needs

- I/O after I/O
- ADCs:
  - Target after target
  - Payload after payload
- What to do after ADCs?
- What if ADCs move to first line?

GOG FOUNDATION®
Transforming the standard of care™

GOG Highlight Reel