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NRG summer seminar
GY cancer review

国立がん研究センター中央病院
腫瘍内科
須藤　一起

2023/8/10

NRG における婦人科がん関連委員会

Descriptions of Gynecologic Cancer Committee

Cervix/Vulvar Cancer Subcommittee

- Cervical cancer – Randomized phase II, Phase II/III, Phase III
- Vulvar cancer – Phase II, Randomized phase II, Phase II/III, Phase III

Ovarian Cancer Subcommittee

- Ovarian cancer (Ovarian cancer = Fallopian tube cancer, Ovarian cancer, Primary Peritoneal Cancer)
- – Neoadjuvant chemotherapy (NACT) – Randomized phase II
- Randomized phase II, Phase II/III, Phase III

Uterine Corpus Cancer Subcommittee

- Endometrial cancer – Randomized phase II, Phase II/III, Phase III
- Uterine sarcoma (leiomyosarcoma) – Randomized phase II, Phase II/III, Phase III
- Gestational trophoblastic neoplasm (GTN)

Rare Tumor Subcommittee

- Clear Cell Tumors/ Germ Cell Tumors/ Ovarian - Low Grade Serous/ Ovarian – Mucinous/ Ovarian - Stromal Tumors

GYN Developmental Therapeutics Committee

- Early phase trials (Phase I, Phase I/II, Phase II), Window of opportunity trials for Cervical cancer/ Endometrial cancer/ Ovarian cancer/ Uterine sarcoma

GYN Phase I Subcommittee

- Safety lead-ins/ Phase I

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婦人科関連委員会のスケジュール
Gynecologic Cancer Committee

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Thursday, July 20, 2023	
2:00 pm – 4:00 pm	Rare Tumor Subcommittee
12:30 pm – 2:30 pm	Developmental Therapeutics Committee
Friday, July 21, 2023	
8:00 am – 10:00 am	Cervix/Vulva Cancer Subcommittee
10:00 am – 12:00 pm	Uterine Corpus Cancer Subcommittee
1:00 pm – 3:00 pm	Ovarian Cancer Subcommittee
4:30 pm – 6:00 pm	Translational Science GYN Cancer Working Group
Saturday, July 22, 2023	
7:45 am – 9:30 am	Gynecologic Cancer Committee

会場：Philadelphia Marriott Downtown Salon GKL/5th Fl.

Acknowledgment: Meeting Agenda, NRG Website, CTEP Website, Ovarian Workshop Chair Dr. Kathleen Moore/ Co-Chair Dr. Joyce Liuから提供いただいたスライド、本発表者メモ等から本スライドを作成。

最近の発表

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ASCO 2023

- **Patient-reported outcomes during pelvic radiation therapy: A secondary analysis on sexual function from NRG-RTOG 1203 (Corrigan et al.)**
  子宮頚癌/体癌対象 急性障害と健康関連QOLに関して、IMRTと従来の骨盤部放射線治療を比較

- **A RPh2 study of olaparib, cediranib, combo of cediranib/olaparib, olaparib/durvalumab, cediranib/durvalumab, and olaparib/capivasertib in recurrent endometorial cancer（NRG-GY012: Multiple Olaparib Combinations in Endometrial Cancer)(Rimel et al.)**

- **Neoplastic and blood-based biomarkers of response in patients with advanced endometrial cancer: Results from NRG GY012 (Makay et al.)**

- **Incorporation of triapine with cisplatin chemoradiation for LACC (locally advanced cervical and vaginal cancer): Results from NRG-GY006, a phase III randomized trial. (Leath et al.)**

Trials open to international Sites

- NRG-GY019 (US, Canada, Korea)
  - A Randomized Phase III, Two-Arm Trial of Paclitaxel/Carboplatin/Maintenance Letrozole Versus Letrozole Monotherapy in Patients with Stage II-IV, Primary Low-Grade Serous Carcinoma of the Ovary or Peritoneum (Amanda Nickles Fader),
  - Activated 8/26/19 Total Accrual 242/457

- NRG-GY026 (US, 1 site at Puerto Rico)
  - A randomized phase II/III trial of paclitaxel/carboplatin alone or combined with either trastuzumab or trastuzumab/pertuzumab in HER2 Positive Stage I-IV uterine serous carcinoma and carcinosarcoma after primary surgery (Erikson, Fader, Santin, Havrilesky QOL)
  - Activated 8/12/22 Total accrual 29/525

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HER2 as a Biomarker in Ovarian + Other GYN Malignancies

Tamara Kalir, M.D., Ph.D. / GYN Pathology
The Icahn School of Medicine at Mount Sinai, N.Y.C.

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Summary criteria for HER2 positivity (likelihood of therapeutic response) by IHC and FISH

	Breast ASCO/CAP 2018	Gastric ASCO/CAP 2016	Endometrial (serous only) CAP recommended
HER2 IHC 3+	>10% circumferential, strong, complete	>=10% strong complete, or basolateral/lateral	>30% strong complete or basolateral /lateral
HER2 FISH amplification	HER2/CEP17 ratio >=2.0 and HER2 signal>=4.0/ nucleus OR ratio <2.0 and HER2 signal >=6.0/nucleus if IHC score 2+ or 3+	HER2/CEP17 ratio >=2.0 OR ratio <2.0 and HER2 signal >6.0/nucleus	HER2/CEP17 ratio >=2.0 No consensus guidelines

ASCO =American Society of Clinical Oncology
CAP = College of American Pathologists

Buza, N. HER2 testing and reporting in endometrial serous carcinoma: practical recommendations for HER2 immunohistochemistry and fluorescent in situ hybridization: proceedings of the ISGyP companion society session at the 2020 USCAP annual meeting. Int. J Gynecol. Pathol. 40:17-23

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What we learned about endometrial serous carcinomas from 2 pre-trial pathology studies:

- ~1/3rd of tumors were HER2 IHC(+)
- IHC-FISH concordance rate was higher when employing a 30% tumor cell IHC staining cut-off compared with a 10% cut-off (86% vs 78%)
- >50% of HER2 (+) tumors showed marked intra-tumoral heterogeneity of HER2 protein expression which correlated with heterogeneity of gene amplification by FISH.

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Re HER2 and Gyn cancers, a promising update from the June 2023 ASCO Annual Meeting reported that “Trastuzumab deruxtecan effectively treats many HER2-expressing cancers”

- Ovarian cancer: ORR of 45% for all patients,

  63.6% for HER2 IHC 3+, 36.8% for HER2 IHC 2+
- Endometrial cancer: ORR of 57.5% for all patients,

  84.6% for HER2 IHC 3+, 47.1% for HER2 IHC 2+
- Cervical cancer: ORR of 50% for all patients,

  75% for HER2 IHC 3+, 40% for HER2 IHC 2+

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Abstract #LBA3000. Lead study author Funda Meric-Bernstam, MDACC

HER2 gene amplification and Next Generation Sequencing (NGS)

- Morsberger et al. (2022) found that all 57 breast cancer patients with HER2 amplification by NGS had concordant results with FISH tests.
- 2023 NCCN guidelines state that NGS may be used for HER2 amplification testing for gastric cancer.
- In ovarian cancer, NGS is already used to identify markers for targeted therapeutics (BRCA, MSI, etc). Possibility for HER2?

Morsberger L, et al. HER2 amplification by next-generation sequencing to identify HER2-positive invasive breast cancer with negative HER2 immunohistochemistry Cancer Cell Int. 2022; 22: 350-359.

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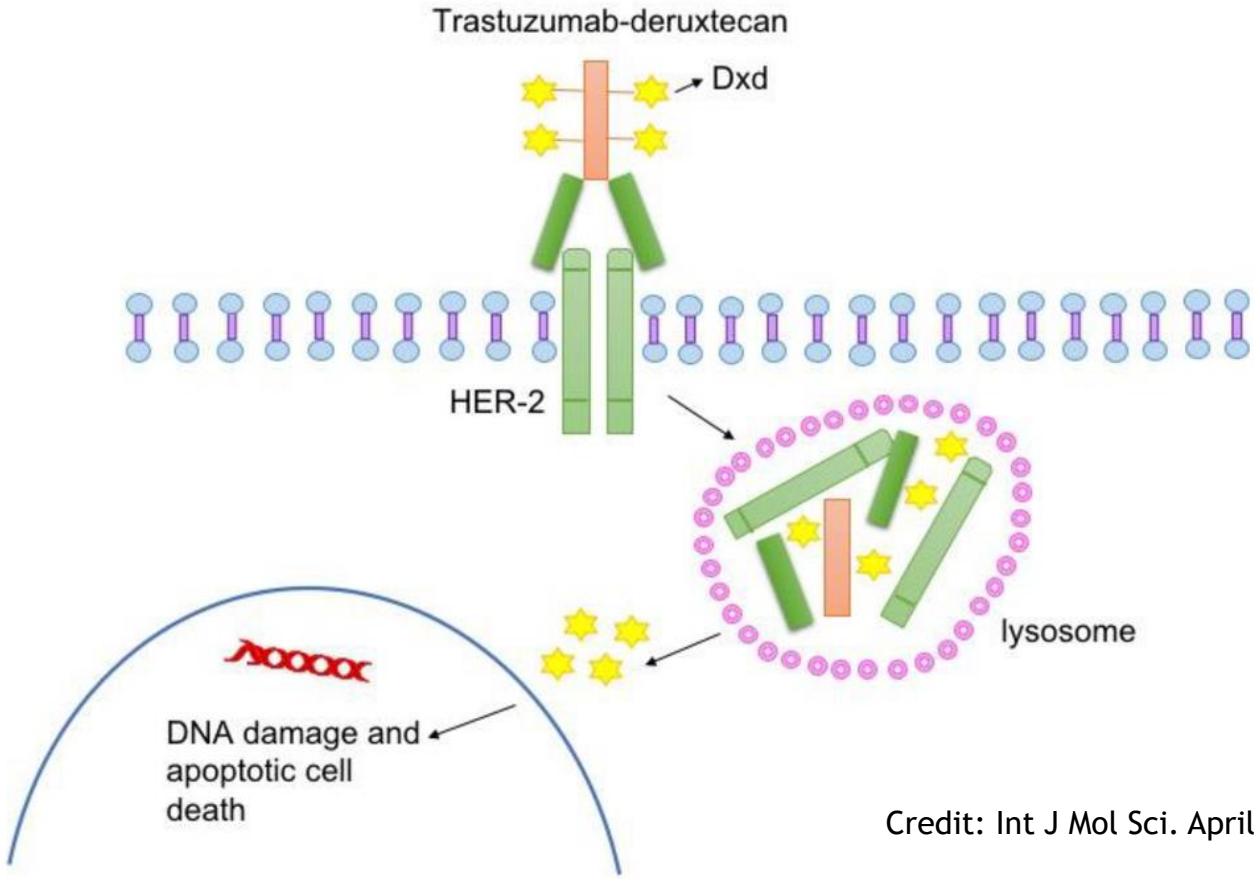
HER2 started out as a biomarker in breast cancer; then it was approved for gastric cancer; now may be the time for its application in pelvic GYN cancers…



F I N I S !

Credit: Int J Mol Sci. April 2021. DOI: 10.3390/ijms22094774. CC

Closed Studies Ovarian Cancer

Primary Manuscript Pending

	Study	Disease situation	Accrual	Comments
1	NRG-GY005	Phase II/III Platinum Resistant Recurrentcediranib/olaparib vs cediranib vs ~~olaparib~~ vs standard chemotherapy	582	Top line results are available
2	NRG-GY007	Phase I/II NACT + Ruxolitinib	147	ASCO 2022
3	NRG-GY009	Phase I/III Platinum Resistant Recurrent PLD/Atezolizumab vs PLD/Bevacizumab/Atezolizumab vs PLD/Bevacizumab	444	
4	NRG-GY021	Phase II Olaparib vs Olaparib Plus Tremelimumab	61	
5	NRG-GY023	Phase II Olaparib/Cediranib/Durvalumab Olaparib/Cediranib Cediranib/Durvalumab Single agent Chemotherapy (non-platinum)	153	ESMO 2023

Closed Studies (Primary Manuscript Published): 213, 262, GY003, GY004
Terminations: 212, 268, 283, GY029

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Biospecimen Access:NRG-GY-TS026 (Hinestrosa, GOG-0136-OV) Distribution in progress

Closed Studies Ovarian Cancer

Primary Manuscript Pending

	Study	Disease situation	Accrual	Comments
Developmental Therapeutics				
1	NRG-GY014	Phase II Tazemetostat	62	
Rare Tumor Subcommittee				
1	GOG-264	Sex Cord Stromal Tumors PC vs BEP	63	IGCS 2020
2	NRG-GY016	Ovarian Clear Cell Carcinoma Pembrolizumab + Epacadostat	14	IGCS 2022

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Ovarian Cancer Subcommittee

Ovarian Cancer Subcommittee

Active Studies: None

Active studyは希少がん、DTのみ。
ここから参加しようという試験無し

Rare Tumor Subcommittee – Ovarian

Active Studies:

a. NRG-GY019, A Randomized Phase III, Two-Arm Trial of Paclitaxel/Carboplatin/Maintenance Letrozole Versus Letrozole Monotherapy in Patients with Stage II-IV, Primary Low-Grade Serous Carcinoma of the Ovary or Peritoneum (Amanda Nickles Fader) Activated 8/26/19 Total Accrual 242/457

GYN Developmental Therapeutics Committee - Ovarian Cancer

Active Studies:

a. NRG-GY027, Phase I/IB Safety and Pharmacodynamic Study of Neoadjuvant (NACT) Paclitaxel and Carboplatin with Ipatasertib as Initial Therapy of Ovarian Cancer PTMA 100805 (Katherine Fuh)

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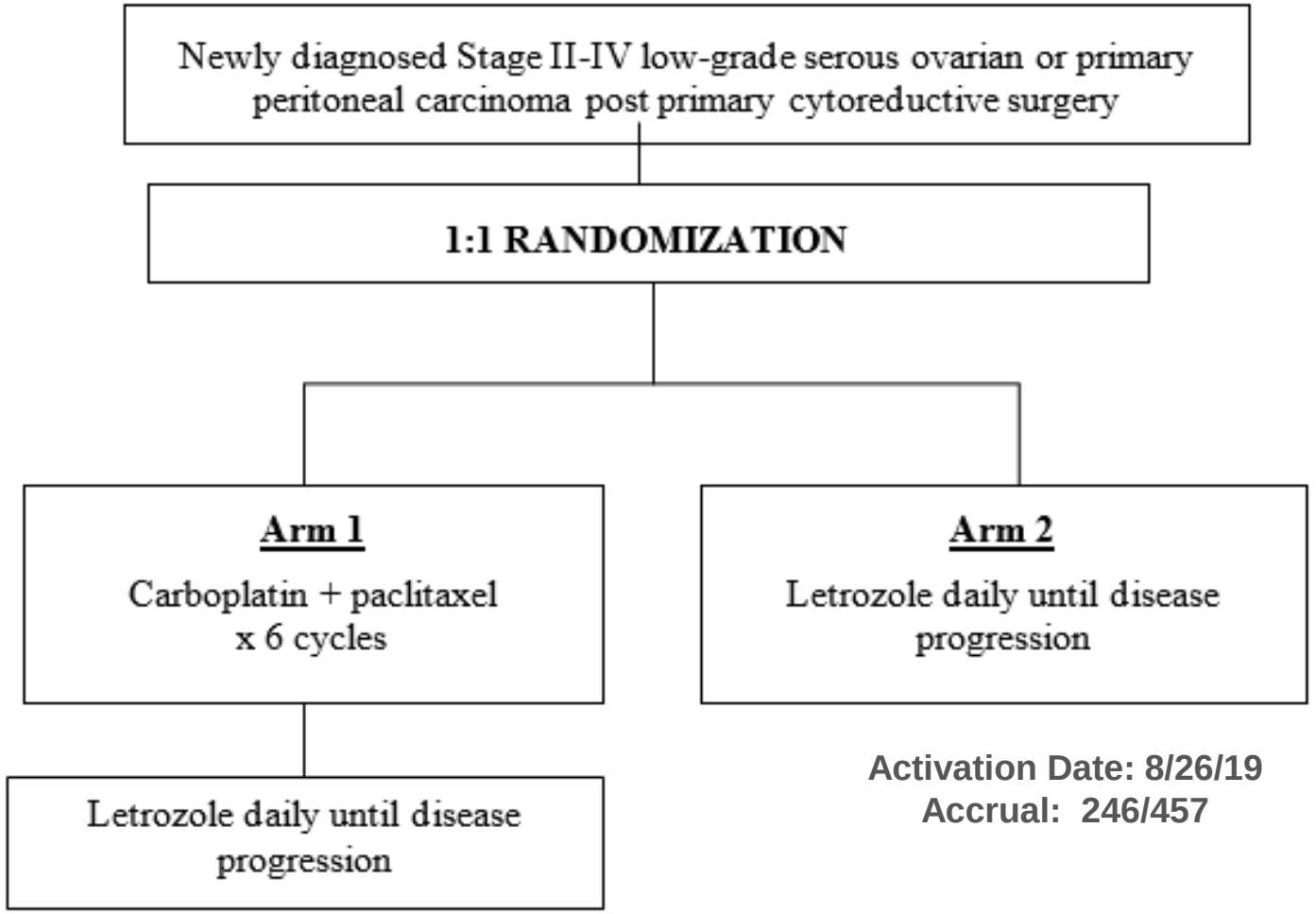
NRG-GY019
Randomized Phase III

- Country
- Residual disease following primary cytoreduction surgery:
  1. microscopic residual disease
  2. any gross residual disease



Activation Date: 8/26/19
Accrual: 246/457

Study Chair: Amanda Fader, MD

Primary Endpoint: Non-inferiority/PFS

NRG-GY027

Women with stage III/IV high grade serous or grade 3 endometrioid ovarian cancer undergoing neoadjuvant chemotherapy (NACT)

Pre-treatment formalin-fixed, paraffin-embedded (FFPE) tumor block collected from laparoscopy (preferred) or five 18G cores (embedded in one block) by radiology/interventional radiology (acceptable) must be available for submission.

Activation Date: 6/27/22
Accrual: 10/24
Temporarily Closed to Accrual

Neoadjuvant Chemotherapy (NACT)
Paclitaxel 175mg/m2 + Carboplatin AUC 5 + Ipatasertib po daily
Every 3 weeks x 3 cycles

Followed by single-agent ipatasertib daily until 24 hours prior to Interval Debulking Surgery (IDS) within 6 weeks of Cycle 3, Day 1

Tissue collection at the time of IDS, to be collected from anatomical site similar to pre-treatment tissue procurement (if possible).

NOTE: Post-operative paclitaxel/carboplatin will be given as per usual care. Dates and doses of post-operative paclitaxel/carboplatin treatments will be collected.

Study Chair: Katherine Fuh, MD, PhD

Developing* Studies Ovarian Cancer

	Study	Disease situation	Comments
1	NRG-GY034 (OV2206)	A Randomized Phase 1/2 Trial Evaluating the Addition of Tolinapant to Weekly Paclitaxel with or without Bevacizumab in Patients with Recurrent Epithelial Ovarian Cancer (Zeligs, Annunziata)	GYN Cancer Committee 2/12/22 OTF 5/20/22, 7/15/22 RSC 10/19/22 X 11/2/22 GCSC 11/16/22, 3/15/23 AOH (3/27/23) ***Protocol UD***
2	OV2238 (OV2135)	Open Label, Multi-Center Phase 1/2 Study of Pegylated Liposomal Doxorubicin/Carboplatin +/- Eltanexor in Patients with Platinum Sensitive Ovarian, Tubal, Peritoneal Carcinoma who received a prior PARP inhibitor for maintenance (Rebecca Arend)	RSC 2/16/22 X 3/2/22 (OV2135) GYN Cancer Committee 10/14/22 OTF 12/16/22, 3/31/23 ***GCSC 7/26/23***
3	OV2307	One vs. Two Years of Maintenance Olaparib, with or without Bevacizumab, in Patients with BRCA1/2 Mutated or Homologous Recombination Deficient (HRD+) Ovarian Cancer Following Response to First Line Platinum Based Chemotherapy (Ying Liu)	GYN Cancer Committee 1/28/23 OTF 3/17/23 RSC 5/10/23 X 5/24/23 ***GCSC 7/26/23***

We're getting close!!!!

Protocol undergoing final revisions and internal reviews Pending pharmacy review and incorporation of SDMC information

Anticipate initial submission to NCI later this summer

オラパリブ
1年 or 2年
意義のあるCQ
で参加しやすい
試験だが、適応
を拡大する試験
ではないので参
加の優先度は低
いか。

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**Developing studies = Approved by NRG RSC but not activated*

Developing* Studies Ovarian Cancer

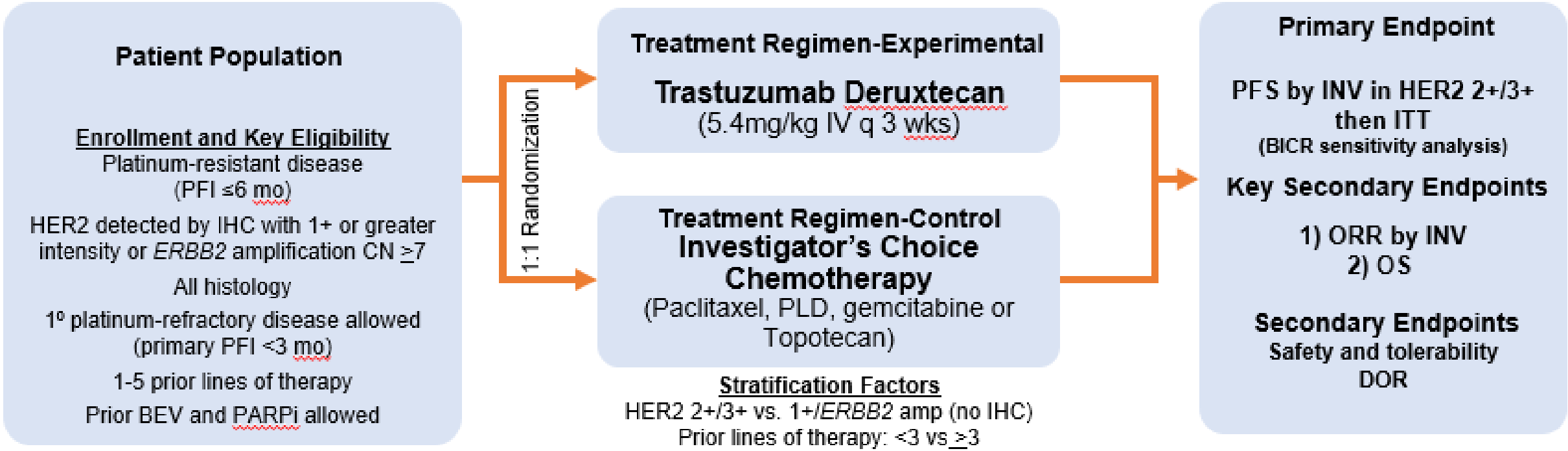
	Study	Disease situation	Comments
Developmental Therapeutics Committee			
1	NRG-GY031 (DT2106)	A Phase 1B study of combination ATR (M1774) and BET inhibition (ZEN-3694) to exploit ARID1A loss in recurrent ovarian and endometrial cancer (Fiona Simpkins)	GYN Cancer Committee 1/30/21 RSC 7/28/21 X 8/11/21 LOI 11/11/21, Approved ***Protocol UD***
Rare Tumor Subcommittee			
1	NRG-GY033 (RT2141)	Phase II Study of Androgen Receptor (AR) Inhibition by Darolutamide in combination with Leuprolide Acetate and Exemestane in Recurrent AR Positive Adult-Type Ovarian Granulosa Cell Tumor (E Hopp, J Rader)	GYN Cancer Committee 10/8/21 RSC 5/18/22 X 6/1/ 22 CrDL LOI 7/18/22, Approved ***Protocol UD***

**Developing studies = Approved by NRG RSC but not activated*

Concepts Ovarian Cancer

	Study	Disease situation	Comments	
Ovarian Cancer Subcommittee				
1	**OV2331**	**Lymphadenectomy In clinically early epithelial ovArian Cancer and survival analysis (LILAC) (Shim)**	**GYN Cancer Committee 7/22/23**	DisAproval Cont. discussion
2	**OV2335**	**Randomized phase 3 trial of the HER2 targeting Antibody Drug Conjugate, Trastuzumab deruxtecan versus investigator choice chemotherapy in recurrent, platinum resistant, HER2+ ovarian cancer (Janco/Moore/Myers)**	**GYN Cancer Committee 7/22/23**	Approval ど真ん中のCQという意味では、進んだ際には候補？
3	**OV2336**	**Randomized Phase III Trial of Bevacizumab + olaparib vs olaparib monotherapy as maintenance in HRD test positive front line epithelial ovarian cancer characterized by KELIM CA-125 kinetics (Dockery/Moore/ Coleman)**	**GYN Cancer Committee 7/22/23**	Disaproval Cont. Discussion
Developmental Therapeutics Committee				
1	**DT2338**	**Repotrectinib and Tiragolumab in Platinum-Resistant and -Refractory Epithelial Ovarian Cancer (Taylor)**	**GYN Cancer Committee 7/22/23**	Support this new concept
Rare Tumor Subcommittee				
1	RT2310	Giredestrant with or without Abemaciclib in Patients with Recurrent Low-grade Serous Carcinoma of the Ovary, Fallopian Tube, or Peritoneum (Lauren Cobb/Brian Slomovitz/David Gershenson)	GYN Cancer Committee 1/28/23 OTF 5/19/23 ***RSC 7/26/23***	Dis Cont
2	RT2321	Exportin 1 inhibitor, eltanexor, in patients with recurrent low-grade serous ovarian carcinoma; a phase II non-randomized study (Dimitrios Nasioudis, Fiona Simpkins)	GYN Cancer Committee 4/14/23	Dis Cont
3	**RT2339**	**A Phase II study of abemaciclib in combination with letrozole in patients with recurrent adult-type ovarian granulosa cell tumor (Cobb/Hillman/Brown)**	**GYN Cancer Committee 7/22/23**	Support this new concept

OV2335 Randomized phase 3 trial of the HER2 targeting Antibody Drug Conjugate, Trastuzumab deruxtecan versus investigator choice chemotherapy in recurrent, platinum resistant, HER2+ ovarian cancer (Janco/Moore/Myers)



This study seeks to demonstrate an improvement in PFS of 45% (HR 0.55) in the HER2 2+/3+ cohort. The assumption for the control arm will be a PFS of 3.6 months, ORR of 16%, and OS of 12 months. This will require a sample size of 170 (for HER2 2+ and 3+)
HER2 IHC test by Gastric ASCO/CAP 2016, Competing trials in other U.S. or **international Groups**.

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Uterine Corpus Cancer Subcommitee

Uterine Corpus Cancer Subcommittee, ACTIVE/RECENTLY CLOSED	Notes
NRG-GY012 A Randomized Phase II Study Comparing Single-Agent Olaparib, Single Agent Cediranib, and the Combinations of Cediranib/Olaparib, Olaparib/Durvalumab (MEDI4736), Cediranib/Durvalumab (MEDI4736), Olaparib/AZD5363 (Capivasertib) in Women with Recurrent, Persistent or Metastatic Endometrial Cancer.: A Platform Trial for Women with Recurrent or Persistent Endometrial Cancer (Mackay, Bender, Westin, Rimel) CTEP IND N=120 (through 6/17/19) N=168 (beginning 8/16/21), Total=288 Stat: Enserro	Closing soon Reactivated 8/16/21 Temp closed 2/22/22 (Safety Lead-in Reactivated 6/13/22 Alert to the approaching accrual target broadcast 5/22/23 and 5/30/23 Integrated (approved): BROCA-HR, angiome 274/288 accrual
NRG-GY018 A Phase III Randomized Placebo-Controlled Study of Pembrolizumab in addition to Paclitaxel and Carboplatin for Measurable Stage III Or IVA, Stage IVB or Recurrent Endometrial Cancer (Eskander) CTEP IND N: 590 pMMR; 220 dMMR = 810 Central MMR testing (NeoGenomics) Stat: Sill/Huang-PRO PRO: Wenzel	NEJM/SGO
NRG-GY020 Randomized phase III trial of radiation +/- pembrolizumab for high intermediate risk mismatch repair deficient (dMMR) endometrioid endometrial cancer (Backes/Cohn) CTEP IND N: 168 (2:1 randomization) Stat: Sill/Huang-PRO PRO: Wright	Closed to accrual.
NRG-GY025 A Randomized Phase II Trial of Nivolumab and Ipilimumab Compared to Nivolumab Monotherapy in Patients with Deficient Mismatch Repair System Recurrent Endometrial Carcinoma (Mahdi) Stat: Sill, N: 90,	Activated 2/7/22, Safety Lead-in (25 pts), Integral (approved): Local MMR IHC +/- MSI Exploratory (not allowed in protocol, requires approval): PD-L1, IFNg, TME, TMB, PBMC exhaustion, TILs, ctDNA sequencing, cytokines 11 enrolled 1 (first patient entered 6/2/22)
NRG-GY026 A randomized phase II/III trial of paclitaxel/carboplatin alone or combined with either trastuzumab or trastuzumab/pertuzumab in HER2 Positive Stage I-IV uterine serous carcinoma and carcinosarcoma after primary surgery (Erikson, Fader, Santin, Havrilesky QOL) Stat: Miller, N: 525,	Open to accrual 8/12/22, Amendment rejected 12/2 and resubmitted 12/4, information still needed from Cell Carta. 29 accrued., Integral (approved): Local HER2 for eligibility, Integrated (requires approval): Central HER2 IHC and ISH
NRG-GY028 A Phase IB and Randomized Phase II Trial of Megestrol Acetate with or Without Ipatasertib in Recurrent or Metastatic Endometrioid Endometrial Cancer (Onstad),Stat: Enserro, N: 18, Developmental Therapeutics Committee, GYN Phase I Subcommittee	Open to accrual at Ph I institutions 1/13/23, 6-18 patients in Phase I, 3 accrued., Integrated (approved): PTEN, ER/PR, WES, RNAseq, PK, Exploratory (approved): pS6/totalS6, pPRAS40/totalPRAS40, PK
Closed Studies, primary manuscript NOT published (Corpus): 238 (IGCS 2022), GY018, GY020, Closed Studies, primary manuscript NOT published (DT): 286B (SGO 2020), Closed Studies, primary manuscript published: 188*, 258, *patient on active treatment	

Uterine Corpus Cancer Subcommittee

New Concepts

a. UC2330, Gemcitabine-docetaxel followed by gemcitabine maintenance vs. Doxorubicin-trabectedin followed by trabectedin maintenance as first-line treatment for metastatic uterine leiomyosarcoma (Hensley/Bose)

b. UC2340, A phase 2 trial of Giredestrant with Abemaciclib in Patients with advanced or recurrent ER+ uterine leiomyosarcoma or other uterine sarcoma with CDKN2A deletion and intact RB1 (Hensley/Bose)
   - 10% (n=23) of uterine sarcomas harbor CDKN2A loss-of-function mutations, which are mutually exclusive with both TP53 and RB1 alterations
   - CDKN2A-deleted/RB1 wild-type uterine LMS derived significant clinical and radiographic benefits from Palbociclib
   - Giredestran is an oral anti-estrogen selective estrogen receptor degrader.

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Uterine Corpus Cancer Subcommitee

Uterine Corpus Cancer Subcommittee Developing Studies	Notes
NRG-GY032 (UC2208) Tailored adjuvant therapy in POLE-mutated and p53-wildtype/NSMP early-stage endometrial cancer (TAPER)/Refining Adjuvant treatment IN endometrial cancer Based On molecular features (RAINBO POLEmut BLUE) **A CCTG trial (Two cohorts: Kuroki, Cosgrove Mentor: Powell)** **Stat: Enserro** **N:** **Uterine Corpus Subcommittee**	GYN Cancer Committee 2/12/22 RSC 2/16/22 Exec 3/2/22 GCSC reviewed 6.16.22, approved 6.30.22. Call w CTEP to discuss review 7.11.22. Team to schedule another call with Lead. 1st draft US appendix to team 8.11.22. Working out logistics via OPEN SDMC w Canadians. Call conducted 11.30.22 to discuss DM/IT interface. Call scheduled 2.1.23 to review drafts w Canadian group. Internal call conducted 2/1/23. Documents back to CCTG with a few questions 3/6/23 Biobanking through CCTG

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Uterine Corpus Cancer Subcommittee (過去の非承認など一部削除)

Uterine Corpus Concepts in development	
UC2043 A Pilot Study of Dactinomycin plus Avelumab as First line Treatment for Selected Patients with Gestational Trophoblastic Neoplasia (Eriksson) Uterine Corpus Subcommittee	GYN Cancer Committee 7/17/20 Tabled. Team continues to work to harmonize with **international trial.**
UC2108 Phase II Study of Androgen Receptor (AR) Inhibition by Darolutamide in Women with Advanced or Recurrent AR Positive ER Low Endometrial Cancer (Kurnit)	GYN Cancer Committee 1/30/21
UC2304 A Phase II De-escalation Trial of PD-1 inhibitor Pembrolizumab for Newly Diagnosed Completely Resected Stage III-IVA Mismatch Repair Deficient (dMMR) Endometrial Cancer (Backes)	GYN Cancer Committee 4/9/21 Resub. for 6/16/23 review (n=75, phase II)
UC2229: Evaluating a Molecular based protocol for EaRly stage high-intermediate risk Endometrial carcinomas directed by ctDNA: The EMERGE-C Trial. (Kuroki, Lee, Pothuri, Secord, Hacker)	
UC2230: Phase II Study of Single-Agent (anti PD-L1) Pembrolizumab in MSI-H Early-Stage Endometrial Cancer Patients Desiring Fertility Preservation. (Covens	
UC2320 Pembrolizumab vs Pembrolizumab in Addition to Paclitaxel and Carboplatin for measurable stage III or IVA, stage IVB, or recurrent Mismatch Repair Deficient Endometrial Cancer (Green , Makker)	
UC2323 Randomized phase III trial of carboplatin, paclitaxel, pembrolizumab, with or without bevacizumab in the treatment of primary, pMMR advanced stage (3 or 4) or recurrent endometrial cancer (Fader)	

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Cervix/Vulvar Cancer Subcommittee

Active Studies:

a. NRG-GY024, Groningen International Study on Sentinel Nodes in Vulvar Cancer (GROINSS-V) III: A Prospective Phase II Treatment Trial (Brian Slomovitz)

Closed Studies, primary manuscript NOT published (Cervix): RTOG-0724, GOG-0263, GOG-0279 (SGO 2023), NRG-GY006 (ASCO 2023)

Closed Studies, primary manuscript NOT published (DT): GY017 (SGO 2022, SGO 2023)

Closed studies, primary manuscript published (Outside Group): 270 (GROINSS-V), THE OUTBACK TRIAL (ANZGOG 0902/GOG 0274/RTOG 1174)

Terminations: None

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Cervix/Vulvar Cancer Subcommittee

New Concepts

a. CV2332, A Phase I/II randomized non inferiority trial of hypofractionated IMRT with concurrent cisplatin and brachytherapy for cervical cancer versus conventional standard of care. (Henson/Moore/Mayadev)

b. CV2333, Phase III study of concurrent cisplatin in combination with paclitaxel versus cisplatin alone during pelvic radiation for cervical cancer (Rose/Amarnath)

c. CV2334, Randomized Phase III trial of HER2 targeting Antibody Drug Conjugate, Trastuzumab deruxtecan versus investigator choice chemo in recurrent, HER2+ cervical cancer previously treated or ineligible for immune checkpoint inhibitors (Washington)

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Cervix/Vulvar Cancer Subcommittee

Studies Under Development

a. CV2220, A Randomized Phase II Study of the Integration of Radiotherapy into Chemotherapy and Pembrolizumab/bevacizumab in Newly Diagnosed Stage IVB Cervical Cancer (Dana Chase)

b. CV2221, A Randomized Phase II Trial of concurrent and adjuvant immunotherapy versus no immunotherapy in high-risk, local regionally advanced cervical cancer (BJ Rimel)

c. CV2305, STRIVE Study: STRatification of Vulvar squamous cell carcinoma by HPV and p53 status to guide Excision (Jessica McAlpine/Amy Jamieson: CCTG, Ritu Salani/Lillian Gien: NRG)

d. CV2308, Induction Chemotherapy followed by Definitive Radiation for Locally Advanced Vulvar Squamous Cell Carcinoma (Emi Yoshida/Jyoti Mayadev)

e. CV2322, Immune Priming with Neoadjuvant Immunotherapy vs. Neoadjuvant Immunotherapy and Chemotherapy vs. Chemoradiation for Locally Advanced Cervical Cancer (Jyoti Mayadev/Dmitriy Zamarin)

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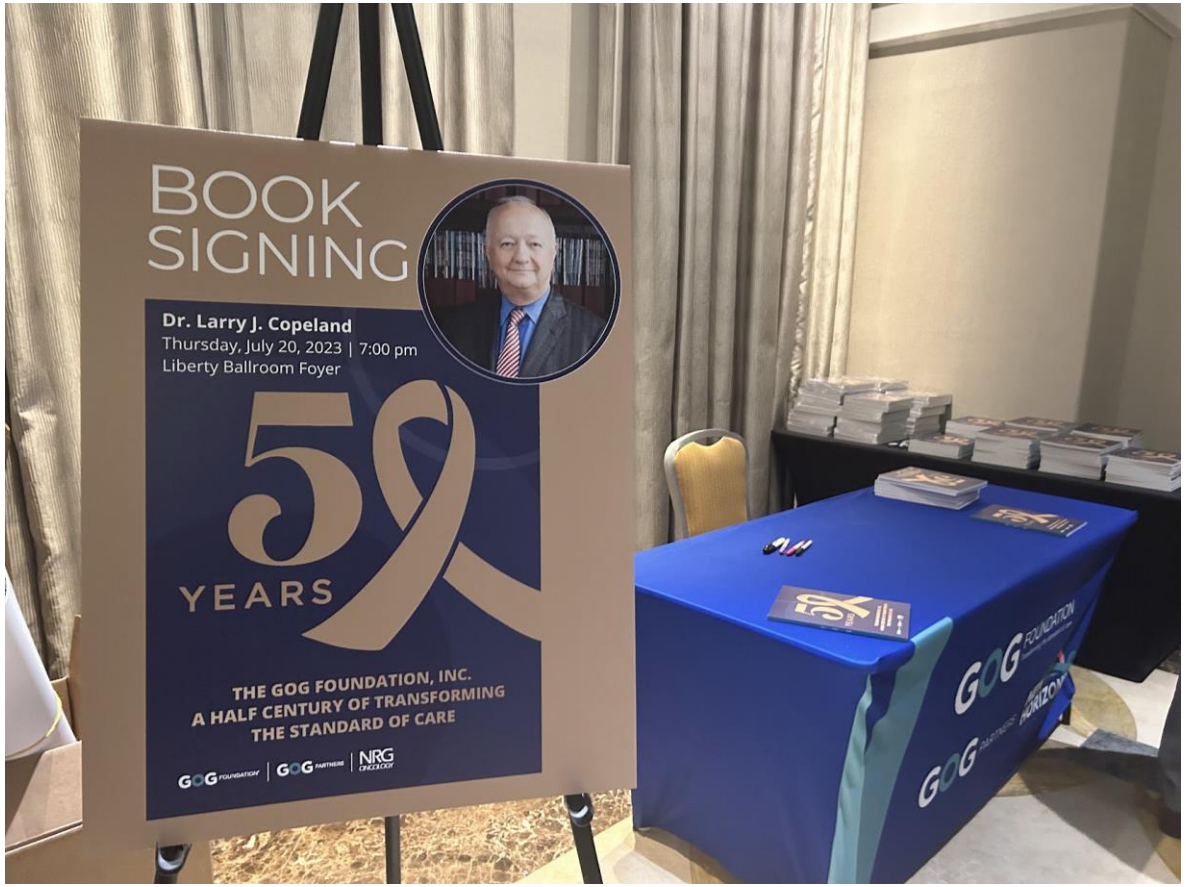
ご清聴ありがとうございました



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Back Ups

最近の発表

NRG ONCOLOGY

Advancing Research. Improving Lives.™

- **Publications:**
- O'Cearbhaill RE, et al. A phase 2 study of dasatinib in recurrent clear cell carcinoma of the ovary: NRG oncology/gynecologic oncology group study 0283. Gynecol Oncol. 2023 Jul 5

- Konski A, et al. Quality-adjusted survival in women with gynecologic malignancies receiving IMRT after surgery: A PRO study of NRG oncology's RTOG 1203. Gynecol Oncol. 2023 Praiss AM, et al. Carboplatin dosing in the treatment of ovarian cancer: An NRG oncology group study. Gynecol Oncol. 2023 Jul;174:213-223.

- Sia TY, et al. The effect of older age on treatment outcomes in women with advanced ovarian cancer receiving chemotherapy: An NRG-Oncology/Gynecologic Oncology Group (GOG-0182-ICON5) ancillary study. Gynecol Oncol. 2023 Jun;173:130-137.

Other NCTN Group Trials & Study Champions

- **A091903**, A Randomized Phase II Trial of Adjuvant Nivolumab with or Without Cabozantinib in Patients with Resected Mucosal Melanoma (Alliance Study Chair: Alexander N. Shoushtari, MD, **NRG Oncology Study Chair & Champion: Danielle Vicus, MD**) **23/99**
- **A092104**, A Randomized Phase 2/3 Study of Olaparib Plus Temozolomide Versus Investigator's Choice for the Treatment of Patients with Advanced Uterine Leiomyosarcoma After Progression on Prior Chemotherapy (Alliance Study Chair: Matthew Ingham, MD, **NRG Oncology Study Chair: Martee Hensley, MD**) **7/70**
- **AGCT1531**, A Phase 3 Study of Active Surveillance for Low Risk and a Randomized Trial of Carboplatin vs. Cisplatin for Standard Risk Pediatric and Adult Patients with Germ Cell Tumors. *This is an Adolescent and Young Adult (AYA) Study: Available to COG and the Adult Groups*. *NRG Oncology Study Champion: Allan Covens* **844/2059**
- **AGCT1532**, A Randomized Phase 3 Trial of Accelerated Versus Standard BEP Chemotherapy for Patients with Intermediate and Poor-Risk Metastatic Germ Cell Tumors. *This is an Adolescent and Young Adult (AYA) Study: It is available to COG and the Adult Groups*. *NRG Oncology Study Champion: Allan Covens* **100/250**
- **S2012**, Randomized Phase II/III Trial of First Line Platinum/Etoposide with or Without Atezolizumab (NSC#783608) in Patients with Poorly Differentiated Extrapulmonary Small Cell Neuroendocrine Carcinomas (NEC). *NRG Oncology Study Champion: Haider Mahdi* **18/189**

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Ovarian Cancer Subcommittee
Review of Closed Studies

Study	Title	Notes
GOG-0212	A randomized phase III trial of maintenance chemotherapy comparing 12 monthly cycles of single agent paclitaxel or CT-2103 (IND#70177) versus no treatment until documented relapse in women with advanced ovarian, primary peritoneal or fallopian tube cancer who achieve a complete clinical response to primary platinum/taxane chemotherapy (Larry J Copeland)	J Clin Oncol 2022
GOG-0213	A phase III randomized controlled clinical trial of carboplatin and paclitaxel (or gemcitabine) alone or in combination with bevacizumab followed by bevacizumab and secondary cytoreductive surgery in platinum-sensitive, recurrent ovarian peritoneal primary and fallopian tube cancer (Robert Coleman)	Lancet Oncol 2017 NEJM 2019
GOG-0262	A randomized phase III trial of every-3-weeks paclitaxel versus dose dense weekly paclitaxel in combination with carboplatin with or without concurrent and consolidation bevacizumab in the treatment of primary stage III or IV epithelial ovarian, peritoneal or fallopian tube cancer (John K Chan)	NEJM 2016
GOG-0273	Chemotherapy toxicity in elderly women with ovarian, primary peritoneal, or fallopian tube cancer (Vivian E von Gruenigen)	Modified dose dense cohort manuscript in draft form
NRG-GY003	Phase II Randomized Trial of Nivolumab with or without Ipilimumab in Patients with Persistent or Recurrent Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancer (Zamarin)	J Clin Oncol 2020
GOG-0281	RP2/3 study to assess efficacy of Trametinib in recurrent or progressive low grade serous ovarian or peritoneal cancer. (David Gershenson)	Presented IGCS 2019 Lancet 2022
GOG-0264	RP2 trial paclitaxel-carboplatin vs BEP for newly diagnosed advanced-stage and recurrent chemo-naïve sex cord stromal tumors of the ovary (Jubilee Brown)	Presented IGCS 2020
NRG-GY004	Phase III Study Comparing Single-Agent Olaparib or the Combination of Cediranib and Olaparib to Standard Platinum-Based Chemotherapy in Women with Recurrent Platinum-Sensitive Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (Joyce Liu and Ursula Matulonis)	Presented ASCO 2020 J Clin Oncol 2022
NRG-GY007	A Phase I/II Study of Ruxolitinib with Front-line Neoadjuvant and Post-surgical Therapy in Patients with Advanced Epithelial Ovarian, Fallopian Tube or Primary peritoneal Cancer. (Chip Landen)	Presented ASCO 2022 Manuscript in circulation

NRG-GY022

Objectives:

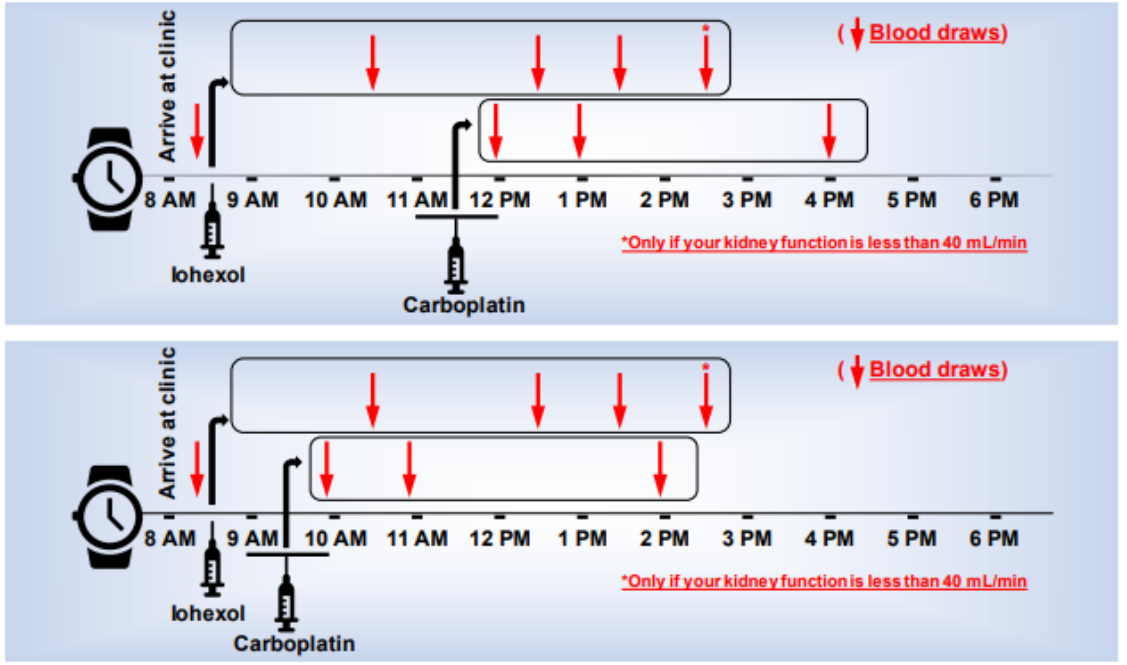
- **Success of targeting carboplatin AUC (using GOG carboplatin dosing Appendix)**
- **Access CG, MDRD-4, CKPD-EPI based on IDMS calibrated serum creatinine in predicting mGRF**
- **Define relationship of mGFR and carboplatin clearance**

SCHEMA

Patients will receive a 5 mL bolus dose of iohexol (Omnipaque 300, contains 647 g/L iohexol corresponding to 300 g/L of organic iodine) soon after they arrive in clinic, with associated blood draws for quantitation of iohexol in plasma at 2, 4, and 5 hours (h) post bolus (and 6 h if renal clearance<40 mL/min, as estimated per local practice).

Next, once patients receive their carboplatin infusion, blood draws for quantitation of plasma ultra-filterable platinum will be obtained 5 minutes (min) before the end of infusion and at 1 and 4 h post end of infusion.

The blood draws for iohexol and carboplatin will occur independently from each other and will overlap in time, e.g. as depicted in figure 1 below.



Activation Date: 11/18/19
Accrual: 243/350

Study Chairs: Sarah Taylor & Jan Beumer

NRG-GY034: A Randomized Phase 1/2 Trial Evaluating the Addition of Tolinapant to Weekly Paclitaxel with or without Bevacizumab in Patients with Recurrent Epithelial Ovarian Cancer

Study Chair: Kristen Zeligs, MD

Study Mentor: Kathleen Moore, MD, MS

Co-Chair/Translational: Christina Annunziata, MD, PhD

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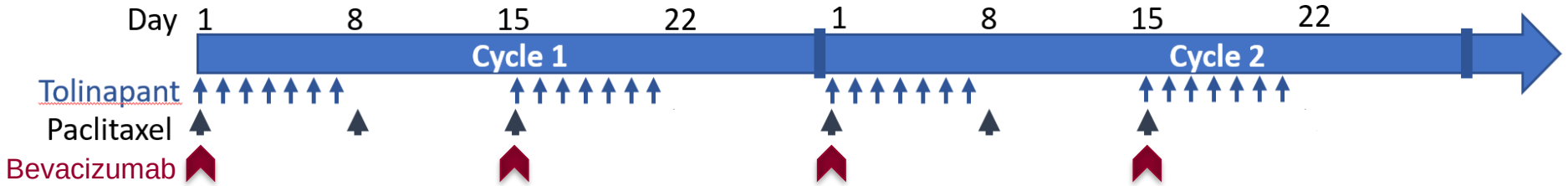
Phase 1 Dose Levels

- Primary endpoints of the DLT will be assessed using BOIN design
- Patient will be enrolled in cohorts with size of 3 with maximum of 9 subjects assigned to each dose level during the dose escalation phase
- Accrual will be increased until a minimum of 12 evaluable patients are treated at the MAD/MTD dose level before proceeding to phase 2



Dose Level	Paclitaxel (IV)	Bevacizumab (IV)	Tolinapant (PO)
-1	60 mg/m^2 for 3 of 4 weeks	10 mg/kg every 2 weeks	120 mg once daily
1	60 mg/m^2 for 3 of 4 weeks	10 mg/kg every 2 weeks	150 mg once daily
2	60 mg/m^2 for 3 of 4 weeks	10 mg/kg every 2 weeks	180 mg once daily
3	80 mg/m^2 for 3 of 4 weeks	10 mg/kg every 2 weeks	150 mg once daily
4	80 mg/m^2 for 3 of 4 weeks	10 mg/kg every 2 weeks	180 mg once daily

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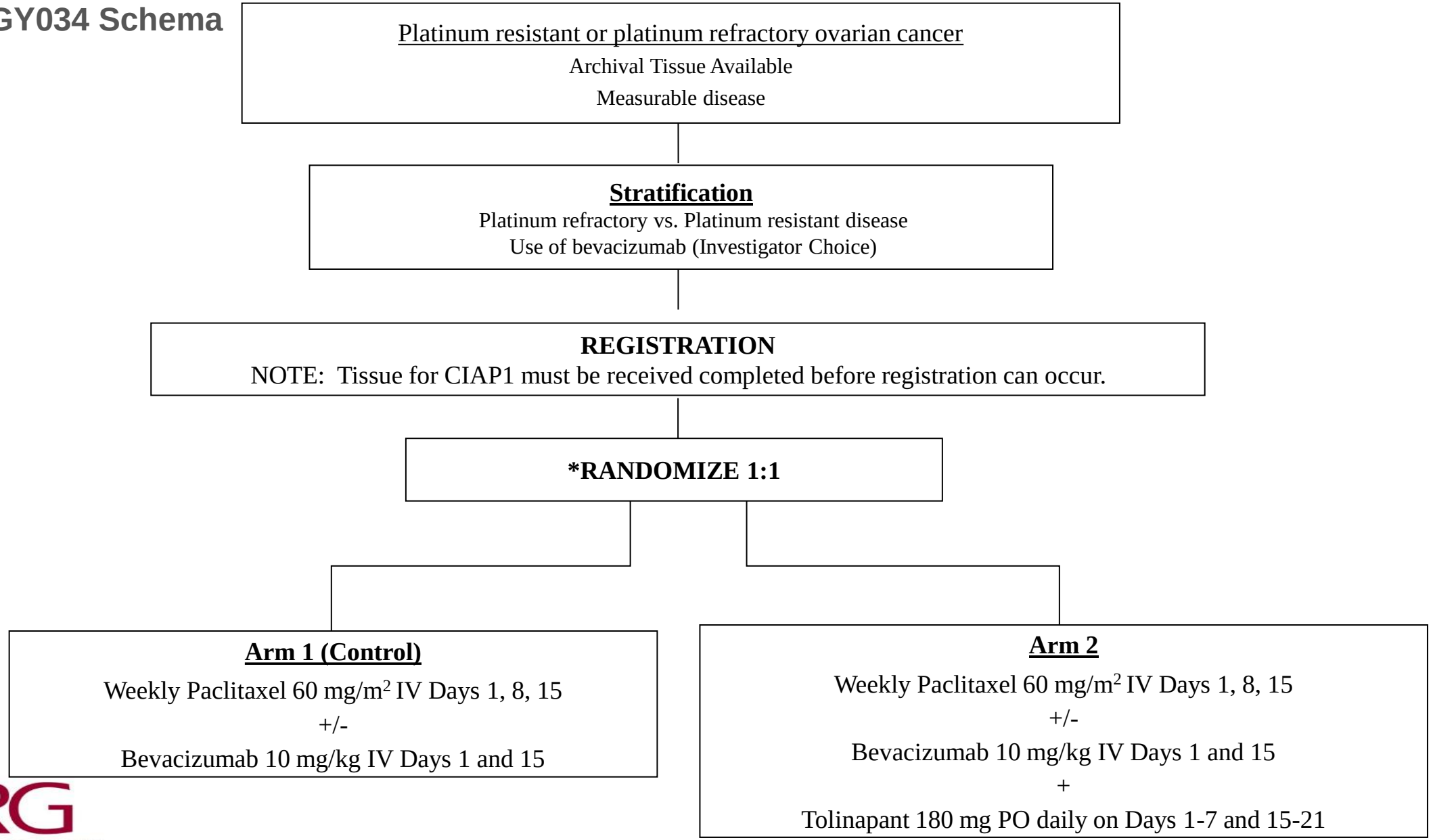
NRG-GY034 Schema



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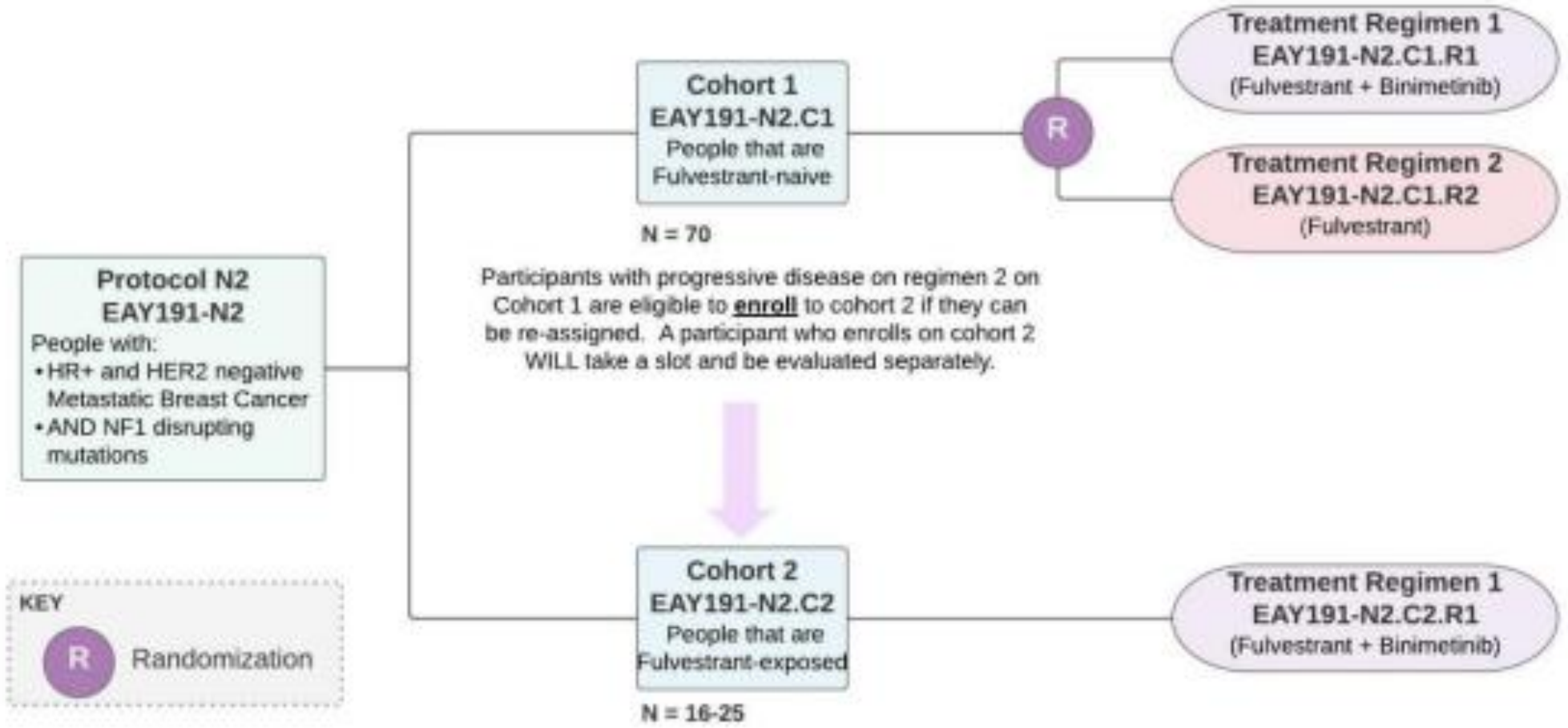
MOLECULAR ANALYSIS FOR COMBINATION THERAPY CHOICE (COMBOMATCH)

NRG ONCOLOGY™

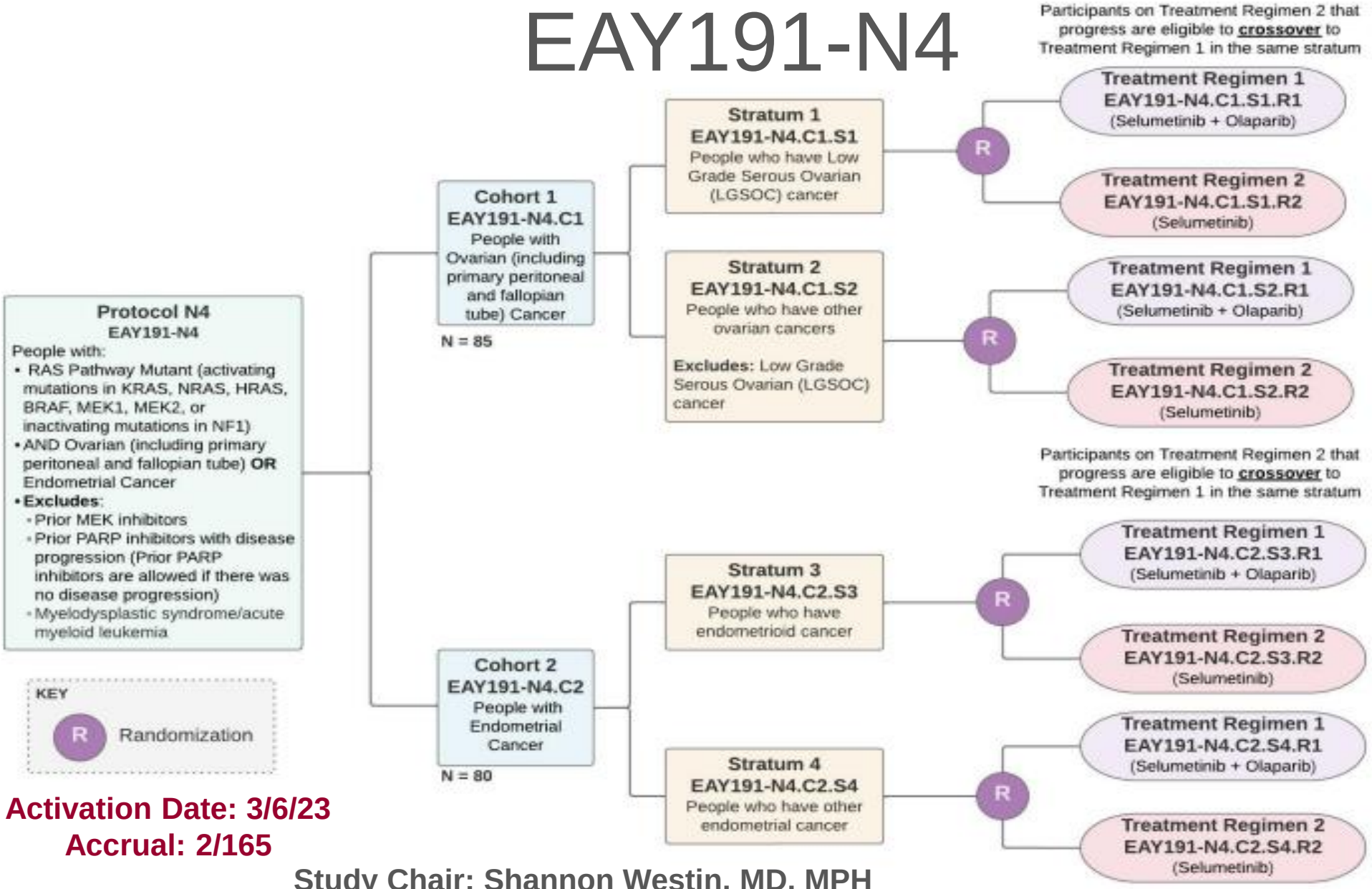
EAY191-N2



Activation Date: 3/6/23
Accrual: 0/95

Study Chair: Bora Lim, MD

EAY191-N4



Activation Date: 3/6/23
Accrual: 2/165

Study Chair: Shannon Westin, MD, MPH

MOLECULAR ANALYSIS FOR COMBINATION THERAPY CHOICE (ComboMATCH)

Study	Agents
EAY191-N5	A randomized trial of neratinib, a pan-ERBB inhibitor, alone or in combination with palbociclib, a CDK4/6 inhibitor, in patients with HER2+ gynecologic cancers and other solid tumors (Haider Mahdi, MD, MPH)

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