The Heartland Association for Gynecologic Oncology (HAGO) is dedicated to providing relevant and timely educational material, a forum for research presentation and collaboration. By bringing gynecologic cancer providers from the central United States together, HAGO strives to collectively work to improve the lives of women with gynecologic malignancies.
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Postoperative venous thromboembolism in gynecologic oncology patients undergoing minimally invasive surgery: Does modality matter?

Authors: 1Matthew K. Wagar, MD, 2Janelle N. Sobecki, MD, MA, 3Thevaa Chandereng, PhD, and 2Sumer K. Wallace, MD

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Objective: Minimally invasive surgery is increasingly utilized for gynecologic cancers. While rates of venous thromboembolism (VTE) after minimally-invasive surgery (MIS) are low, comorbidity such as obesity, and poor performance status are prevalent in women with gynecologic cancer and may increase risk of perioperative VTE. Currently, multiple guidelines exist regarding extended VTE prophylaxis for patients undergoing MIS for gynecologic cancers. Our primary objectives were to determine incidence and risk factors for postoperative VTE in patients undergoing MIS for gynecologic cancers, and to determine differences in the incidence of VTE by MIS modality.

Methods: We performed an IRB-approved, retrospective cohort study of all patients undergoing MIS (robot-assisted, traditional laparoscopy, single-port laparoscopy) for gynecologic cancers between January 2014 and December 2018. We collected demographic and perioperative data (operating room (OR) time, administration of intra-operative and post-operative VTE prophylaxis) using electronic medical records. Chi-square, Fisher’s exact test, and one-way ANOVA were performed to determine risk factors related to VTE occurrence.

Results: 485 patients were included with mean age 61 and mean BMI of 36. Most had uterine cancer (83%) and the majority of cancer diagnoses were early stage (Stage I, 81%). No VTE events were identified within 30 days following surgery. VTE was diagnosed in 6 patients in the postoperative period (1.2%, median time to VTE 16 months). Of those diagnosed with postoperative VTE, 4 had an additional risk factor (Factor V Leiden, IVC compression, atrial fibrillation, tamoxifen use). Incidence of VTE did not differ between MIS modalities. Age, smoking status, BMI, cancer type, stage and OR time were not significant risk factors for postoperative VTE.

Conclusion: The incidence of postoperative VTE in patients with gynecologic cancers undergoing MIS is low overall and does not differ by modality. Extended postoperative prophylactic anticoagulation would not have prevented VTE in the immediate postoperative period in our population. Extended VTE prophylaxis may be warranted in patients with additional risk factors, however, further research is needed to determine efficacy and duration.
Patient outcomes following robotic radical hysterectomy in women with early stage cervical cancer: a retrospective analysis of outcomes from a high-volume robotic surgical program

Authors: Sarah L Todd, MD, Taylor M Hodge, MD, Rebecca C Pierson, MD, Jeremy T Gaskins, PhD, and Daniel S Metzinger, MD

Objectives: Recent data suggests that minimally-invasive approaches (conventional laparoscopic and robotic) to radical hysterectomy for early stage (FIGO 2009 stages IA1, IA2, IB1, IB2) cervical cancer may be associated with decreased disease-free survival as compared to the abdominal approach. Notably, the robotic approach is underrepresented in these studies. Our study sought to determine disease-free survival and recurrence rates in patients with early stage cervical cancer who underwent robotic radical hysterectomy in a high-volume robotic surgery center.

Methods: In this retrospective case series, disease-free survival was analyzed following robotic radical hysterectomy for patients with early stage cervical cancer at a single institution. Data were abstracted from the medical records of all cases conducted between 2010 and 2018, and only women with stage I cervical cancer who underwent robotic radical hysterectomy as sole treatment modality were included. Of importance, no abdominal or conventional laparoscopic radical hysterectomies were conducted at this institution between these dates. Due to a lack of progression events, data could not be analyzed using usual survival statistics. Survival rates were estimated at clinically important time points, and confidence intervals were estimated at each using the Agresti-Coull method, considering only those who were at risk at the time point.

Results: In total, 74 patients who underwent robotic radical hysterectomy for cervical cancer were identified, of whom 37 met criteria for inclusion in our study based on complete medical records and solely surgical management. To date, no recurrences have been identified in any of these 37 patients.

Conclusions: In our study, no episodes of disease recurrence were identified, suggesting that a robotic approach to radical hysterectomy may not adversely affect patient outcomes when performed by an experienced robotic surgeon. Future studies incorporating data from other large-volume robotic centers are warranted prior to abandoning the robotic radical hysterectomy. Exploration of survival differences amongst patients undergoing radical hysterectomy via abdominal versus robotic approach from a mechanistic standpoint needs to be pursued to determine whether sacrificing the reduction in morbidity associated with the robotic approach is in the best interest of patients.

Disclosures: Dr. Daniel Metzinger consults for Johnson&Johnson and Google
Surgical debulking improves survival in high-grade serous carcinoma regardless of platinum sensitivity

Authors: Rei Christian Salinas Calma, Nicholas D. Cardillo, Yasmin A. Lyons, Michael J. Goodheart, Jesus Gonzalez-Bosquet

Objectives: Optimal cytoreduction and platinum sensitivity are both important predictors of survival in ovarian cancer. The question remains, however, whether optimal cytoreduction benefits patients with poor response to chemotherapy as well as those with longer periods of progression-free survival. We aimed to assess whether patients who underwent primary optimal cytoreduction experienced improved survival regardless of platinum sensitivity.

Methods: We performed a retrospective, case-control study using our institution’s ovarian cancer database to evaluate the effect of optimal cytoreduction on advanced stage, high grade serous ovarian cancer. Patients’ characteristics were compared using logistic regression and both univariate and multivariate Cox-Proportional Hazard Regression. Validation of the model was then performed within the TCGA database.

Results: A total of 470 patients were assessed for inclusion. 234 patients were included as responders to chemotherapy and 98 were included as non-responders. Significant survival characteristics were identified and included in the multivariate analysis. Figure 2 demonstrates independent predictors of survival. Kaplan-Meier survival curves showed improved survival both for patients who were responders to chemotherapy as well as optimal cytoreduction (Figure 3; p<0.001). Log-Rank analysis demonstrated improved survival for patients receiving optimal cytoreduction among both non-responders and responders (p<0.001).

Conclusions: Our analysis shows that patients who undergo primary optimal cytoreduction have a survival benefit regardless of their response to chemotherapy. Our model is well validated within the TCGA database. Therefore, optimal primary cytoreduction should be considered, even in patients with advanced disease. If we are able to someday predict response to chemotherapy in patients, cytoreductive surgery should still be considered a part of the treatment of non-responders.
Fig 2: Significant variables in the survival univariate analysis (p<0.05) were introduced in the Multivariate analysis. The complexity index score was used to synthesize all surgical procedures in a single score. In parenthesis are reference values for the variables: The older the patient, the less survival. Patients that had suboptimal surgery and did not respond to chemotherapy had worse survival. Patients with more cycles of chemotherapy (up to 6) had more survival. Patients that underwent Neoadjuvant chemotherapy had less survival.

Fig 3: (A) Survival curves comparing patients who respond to chemotherapy vs. those who do not; p<0.001. (B) Survival curves comparing those undergoing primary optimal vs. suboptimal cytoreductive surgery; p<0.001. (C) Survival curves evaluating the combination of response to chemotherapy and results of cytoreduction. Responders to chemotherapy who underwent optimal cytoreduction had the best survival. Non-responders undergoing sub-optimal surgery had the worst.
Immunophenotyping of tumor microenvironment to uncover the hidden clues for Immunotherapy response in Ovarian Cancer

Authors: S. Talukdar\textsuperscript{a}, J. Cepela\textsuperscript{a}, Z. Chang\textsuperscript{a}, Y. Zhang\textsuperscript{a}, A. Grad\textsuperscript{b}, S.A. Mullany\textsuperscript{c}, Andrew Nelson\textsuperscript{d}, T. Starr\textsuperscript{b} and B. Winterhoff\textsuperscript{b}.

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Objectives: Robust biomarkers to predict immunotherapy response in ovarian cancer (OC) have remained elusive. To better understand the immune landscape of OC microenvironment and to develop predictive biomarkers to select candidates for immune therapy, we have initiated a prospective study to comprehensively analyze the unique molecular and histopathological characteristics of tumor samples taken during primary debulking, interval debulking and at recurrence.

Methods: We have enrolled over 40 women and have completed single cell RNA sequencing (scRNAseq), multiplex immunohistochemical assays, H&E scoring for tumor infiltrating lymphocytes (TILs) and NanoString molecular subtyping in 30 women. ScRNAseq was performed using the 10X genomics platform and raw sequencing data was processed using multiple bioinformatics methods, including ccFindR, Seurat, SC3, ClusterExperiment, and CIDR. Gene expression patterns, prevalence and expression levels of co-stimulatory molecules, programmed cell death protein and its ligand-1, PD-1 and PDL-1 were analyzed. TILs scoring was performed using Salgado scoring criteria and PDL-1/PD-1 IHC staining was assessed based on Tumor proportion score (TPS) and Combined Proportion score (CPS).

Results: ScRNAseq revealed PD-1 and PDL-1 genes in 23/70 (76\%) patients across some cell types (% expression range: 1-22\%) while 20/30 (66\%) showed expression both in immune and epithelial cells. Highest expression of both genes was noted in 4/30 (12\%) patients. PDL-1 gene levels by ScRNAseq demonstrated robust linearity across high and low expression ranges noted on IHC assays. ScRNA-seq demonstrated an added advantage of being able to detect genes on tumor samples with absent PDL-1 IHC staining. Differential expression of PD-1/PDL-1 genes among 4 molecular subtypes showed highest expression level in immunoreactive group. Interestingly, 2 patients in this group showed absence of these genes indicating that molecular subtyping alone might not be predictive of immunotherapy response. Stromal TILs of 50-90\% and 20-40\% were observed in 4/30 (13\%) and 10/30 patients (33\%) respectively, although no correlation was noted between TIL scoring and level of PD-1/PDL-1 genes.

Conclusions: Single-cell RNA-seq is more reliable in identifying PD-1/ PDL-1 across cells than IHC assays. Single biomarker alone might not be predictive of treatment
response. Our study is ongoing and we will categorize these patients into various subtypes based on presence or absence of multiple immune markers (PD-1/PDL-1, TILs, molecular subtypes, IHC assays) and will follow the disease course in these categories. This could help identify patients most likely to benefit from immunotherapy in the future and further understand the mechanism of immune evasion in OC.
Single cell analysis reveals ovarian cancer subpopulations contributing to recurrence

Authors: Z. Chang\textsuperscript{a}, S.M. Bedella\textsuperscript{b}, L.D. Uppendahl\textsuperscript{a}, Y. Zhang\textsuperscript{a}, A. Grad\textsuperscript{b}, J. Wang\textsuperscript{b}, S.A. Mullanyc, A.C. Nelson\textsuperscript{a}, T. Starr\textsuperscript{b} and B. Winterhoff\textsuperscript{b,c}\textsuperscript{*}

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Objectives: Demonstrate a novel precision medicine approach in the diagnosis and treatment of ovarian cancer through comprehensive genomic and molecular analysis of a BRCA1+ primary, recurrent, patient-derived xenograft (PDX), and chemotherapy resistant PDX tumor.

Methods: The patient was consented as part of a prospective precision medicine study in ovarian cancer utilizing single cell sequencing technology. A tumor specimen at the time of primary debulking was obtained for single cell RNA (scRNAseq), single cell exome, bulk exome, and RNA sequencing. Portions were also used to create PDX mouse models, which were treated with chemotherapy to generate resistant PDX tumors. These PDX tumors, as well as tumor collected at the time of the patient’s platinum sensitive recurrence, were analyzed using scRNAseq. The patient also underwent genetic counselling with subsequent germline medical exome sequencing (covering \textasciitilde 5000 genes).

Results: The patient’s known BRCA1 founder mutation, 187delAG, was confirmed by somatic single cell exome sequencing and germline exome analysis. No additional clinically relevant mutations were identified via the extended germline panel. scRNAseq was able to identify two subpopulations within the primary patient tumor that led to her clinical recurrence. Two similar populations in the primary PDX tumors were identified as well. These populations are enriched for ribosomal proteins, and targets of CEBPB, MYC, and PML transcription factors.

Conclusions: We have created a compilation of single cell data on a BRCA1+ patient and identified, for the first time, chemotherapy resistant cancer cell populations in the primary ovarian tumor and matching PDX tumor which persist after chemotherapy. Further study of these subpopulations may guide novel treatment approaches for adding targeted treatment during upfront therapy in order to improve patient outcomes.
Association of fusion genes with optimal surgical outcome and survival in high grade serous ovarian cancer

Authors: Andreea Newtson; Henry Reyes; Yasmin Lyons; Nicholas Cardillo; Eric Devor; Michael Goodheart; Jesus Gonzalez-Bosquet

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Objectives: Fusion genes result from chromosomal rearrangements leading to the formation of fusion transcripts. Many fusion genes have been associated with oncogenesis, such as BCR-ABL1 in chronic myelogenous leukemia. However, little is known of their role in the natural history and prognosis in high grade serous ovarian cancer (HGSC). To explore this, we compared the presence of fusion genes between normal fallopian tubes and HGSC. Then, we assessed the association of fusion genes with surgical outcomes and survival in HGSC.

Methods: RNA from 112 HGS and 12 normal fallopian tube specimens from our Biobank tissue repository was purified and sequenced. Sequencing was carried out on the Illumina HiSeq4000 platform using 150 bp paired-end transcripts. Reads were mapped and aligned against version GRCh38 of the human genome. The suite STAR was used to identify and validate \textit{(in silico)} fusion genes. Logistic regression was used to compare fusion genes between normal fallopian tubes and HGSC and to associate fusion genes with clinical outcomes, such as optimal cytoreduction. Association of fusion genes with survival was assessed via Cox proportional hazard ratios.

Results: Fusion gene RN7SKP71--RN7SKP48 between chromosomes 12 and 4 was present in all tube and HGSC samples. Fusion gene AC026191--RGAP3 was present in more normal fallopian tubes than in HGSC samples (\(p=0.009\)). This fusion was also independently associated with poor surgical outcomes in multivariate analysis (\(p=0.039\)). Altogether, there were 8 fusion genes independently associated with worse survival, even after adjusting for other clinical variables. Fusion gene NRIP1--AJ009632.2 specifically had the worse prognosis with a risk of death 40+ times greater than the reference.

Conclusions: Fusion genes can be used to assess clinical outcomes in HGSC. More research is needed to investigate whether these fusion genes have a role in the natural history of HGSC and could be used for prognostication.
Role of Collagen Fiber Morphology on Ovarian Cancer Cell Migration Using Image-Based Models of the Extracellular Matrix

Authors: Samuel Alkmin¹, Rebecca Brodziski¹, Haleigh Simon¹, Daniel Hinton², Randall H. Goldsmith², Manish Patankar³ and Paul J. Campagnola¹

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Objectives: Remodeling of the extracellular matrix is an important part in the development and progression of many epithelial cancers. However, the biological significance of collagen alterations in ovarian cancer has not been well established. In this work, we investigated the role of collagen fiber morphology on cancer cell migration using tissue engineered scaffolds based on high resolution Second Harmonic Generation (SHG) images of ovarian tissues.

Methods: The collagen-based scaffolds are fabricated by multiphoton excited (MPE) polymerization, which is a freeform 3D method affording submicron resolution feature sizes (~0.5 μm). This capability allows the replication of the collagen fiber architecture, where we constructed models representing normal stroma, high risk tissue, benign tumors, and high-grade tumors. These were seeded with normal and ovarian cancer cell lines to investigate the separate roles of the cell type and matrix morphology on migration dynamics.
**Results:** The primary finding is that key cell-matrix interactions such as motility, cell spreading, f-actin alignment, focal adhesion and cadherin expression are mainly determined by the collagen fiber morphology to a larger extent than the initial cell type. Moreover, we found these aspects were all enhanced for cells on the highly aligned, high grade tumor model. Conversely, the weakest corresponding responses were observed on the more random mesh-like normal stromal matrix, with the partially aligned benign tumor and high-risk models demonstrating intermediate behavior.

**Conclusions:** Using MPE, we constructed image-based models of ovarian tissues. This technique is superior to other fabrication methods as the complex morphology of the collagen visualized by SHG microscopy can be recapitulated with high fidelity. The key finding is that cell characteristics such as motility, cell shape, f-actin alignment, focal adhesion expression, and cadherin expression are mainly determined by the collagen fiber morphology to a larger extent than the initial cell type. These results are all consistent with a contact guidance mechanism. The models cannot be synthesized by other conventional fabrication methods and we suggest this approach will enable a variety of studies in cancer biology.
Patient-reported outcomes (PROs) in patients (pts) receiving niraparib in the PRIMA/ENGOT-OV26/GOG-3012 trial

Authors: William H. Bradley,1 Bhavana Pothuri,2 Sileny Han,3 Dana Chase,4 Florian Heitz,5 Robert Burger,6 Lydia Gaba,7 Linda Van Le,8 Eva Guerra,9 David Bender,10 Jacob Korach,11 Noelle Cloven,12 Philippe Follana,13 Jean-François Baurain,14 Carmela Pisanò,15 Ulla Peen,16 Johanna Maenpaa,17 Emeline Bacque,18 Yong Li,18 Antonio González-Martin,19 Bradley J. Monk4

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Objectives: Niraparib is a poly(ADP-ribose) polymerase (PARP) inhibitor that is approved for use in heavily pretreated pts and as maintenance treatment of pts with newly diagnosed or recurrent ovarian cancer following a response to platinum-based chemotherapy (CT). Here we report PROs in pts receiving niraparib and placebo (PBO) in the PRIMA/ENGOT-OV26/GOG-3012 trial.

Methods: This double-blind, PBO-controlled, phase 3 study randomized 733 pts with newly diagnosed advanced ovarian, primary peritoneal, or fallopian tube cancer with a complete or partial response (CR or PR) to first-line (1L) platinum-based CT. Pts received niraparib or PBO once daily for 36 months or until disease progression. The primary endpoint was progression-free survival (PFS) assessed by blinded independent central review. PROs, a secondary endpoint, were collected every 8 weeks for 56 weeks, then every 12 weeks thereafter while treatment was ongoing. Once a pt discontinued treatment, PRO evaluations were performed at the time of treatment.
discontinuation and then at 4, 8, 12, and 24 weeks (±1 week for each time point) after the end of treatment, regardless of the status of subsequent treatment. The validated PRO instruments utilized were FOSI, EQ-5D-5L, EORTC-QLQ-C30, and EORTC-QLQ-OV28.

**Results:** Compliance rates were >80% for all of the PRO instruments used in the study. PRO analysis of the EORTC-QLQ-C30 and EORTC-QLQ-OV28 did not indicate a difference in health-related quality of life scores of pts treated with niraparib vs placebo. Mean scores between niraparib and placebo arms were similar at each time point. Overall, the health utility index showed a slight improvement trend in pts who received niraparib vs placebo.

**Conclusions:** Consistent with PRO results in the NOVA study, pts receiving niraparib in the PRIMA trial did not experience a decrease in quality of life compared with those receiving placebo.

**Disclosures:**

WHB: Dr. Bradley has nothing to disclose.

BP: Dr. Pothuri reports grants, personal fees and non-financial support from Tesaro; and advisory board fees from AstraZeneca and Clovis Oncology.

SH: Dr. Han has nothing to disclose.

DC: Dr. Chase reports speakers’ bureau fees from Tesaro/GSK.

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LG: Dr. Gaba has nothing to disclose.

LVL: Dr. Van Le has nothing to disclose.

EG: Dr. Guerra reports consulting fees, advisory board fees, and travel support from Roche; consulting and advisory board fees from Clovis Oncology, Tesaro, PharmaMar, AstraZeneca, Merck Sharp & Dohme, and GlaxoSmithKline; and travel support from Baxter and GlaxoSmithKline/Tesaro.

DB: Dr. Bender has nothing to disclose.

JK: Dr. Korach has nothing to disclose.

NC: Dr. Cloven has nothing to disclose.

PF: Dr. Follana has nothing to disclose.

J-FB: Dr. Baurain has nothing to disclose.

CP: Dr. Pisano has nothing to disclose.

UP: Dr. Peen has nothing to disclose.

JM: Dr. Maenpaa reports Honoraria from Tesaro, AstraZeneca, Clovis, Roche, MSD and OrionPharma.

EB: Dr. Bacque is an employee of GlaxoSmithKline.

YL: Dr. Li is an employee of GlaxoSmithKline.
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**Encore statement:** This data is presented on behalf of the original authors with their permission. Presented at Oncology Nursing Society (ONS) virtual meeting, April 29-May 3 in San Antonio, TX (abstract #7612).
Evaluation of an individualized starting dose of niraparib in the PRIMA/ENGOT-OV26/GOG-3012 study

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Objectives: Niraparib is approved at a fixed starting dose (FSD) of 300 mg QD for maintenance treatment of patients (pts) with recurrent ovarian cancer (OC) achieving a complete or partial response to platinum-based chemotherapy based in the ENGOT-OV16/NOVA study. A post-hoc analysis of NOVA showed baseline bodyweight (BW) and platelet count (PC) were predictive for hematologic toxicities and dose reductions. Following this analysis, the PRIMA/ENGOT-OV26/GOG-3012 study was amended to prospectively evaluate the safety and efficacy of an individualized starting dose (ISD) regimen.

Methods: This double-blind, placebo-controlled, phase 3 study randomized 733 pts with newly diagnosed advanced OC with a complete or partial response to first-line (1L) platinum-based chemotherapy. The protocol was amended to change the dose from 300 mg FSD for all patients to an ISD regimen: 200 mg QD in pts with BW <77 kg and/or PC <150,000/µL or 300 mg QD in pts with BW ≥77 kg and PC ≥150,000/µL. Exposure, efficacy, and safety data were compared between patients treated with FSD vs ISD.
**Results:** Efficacy in the ISD subgroup was comparable to the FSD subgroup relative to placebo (Table). An interaction test showed no treatment difference between ISD and FSD at the pre-specified 0.10 significance level ($p=0.30$). Medians for dose intensity and relative dose intensity in pts who received niraparib were similar. The overall safety profile among pts in the niraparib arm ($n=484$), including grade ≥3 hematologic toxicities, improved with the ISD.

**Conclusions:** The ISD in the 1L maintenance setting provides comparable efficacy to the FSD while reducing the risk of hematologic toxicities. No new safety signals were identified.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Fixed Starting Dose (300 mg) N=475</th>
<th>Individualized Starting Dose (200 or 300 mg) N=258</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard ratio</td>
<td>0.59</td>
<td>0.69</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.46–0.76</td>
<td>0.48–0.98</td>
</tr>
<tr>
<td>Dose intensity*</td>
<td>n=315</td>
<td>n=169</td>
</tr>
<tr>
<td>Median, mg/day</td>
<td>181.8</td>
<td>178.6</td>
</tr>
<tr>
<td>Median, relative, %</td>
<td>60.6</td>
<td>66.4</td>
</tr>
<tr>
<td>Grade ≥3 hematologic toxicities b n (%)</td>
<td>Niraparib n=315</td>
<td>Placebo n=158</td>
</tr>
<tr>
<td>Thrombocytopenia event</td>
<td>152 (48)</td>
<td>36 (21)</td>
</tr>
<tr>
<td>Anemia event</td>
<td>112 (36)</td>
<td>38 (22)</td>
</tr>
<tr>
<td>Neutropenia event</td>
<td>75 (24)</td>
<td>25 (15)</td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Combined clinical and laboratory events.

**Disclosures:**

WHB: Dr. Bradley has nothing to disclose.

MRM: Dr. Mirza reports personal fees and other from Karyopharm Therapeutics, Sera Prognostics; grants and personal fees from AstraZeneca, Clovis Oncology, Pfizer, Tesaro; personal fees from Genmab, BioCad, Sotio, Geneos Therapeutics, Merck, Oncology Venture, Seattle Genetics, Sera Prognostics, Takeda Pharmaceutical Company Ltd, Zailab; and grants from Boehringer Ingelheim.

AGM: Dr. González-Martín reports personal fees and non-financial support from AstraZeneca; grants, personal fees and non-financial support from Tesaro and Roche Holding AG; and personal fees from Clovis Oncology, Merck & Co. Inc., Genmab, Immunogen, PharmaMar S.A, and Oncoinvent AS.

WG: Dr. Graybill reports personal fees from Tesaro.

DMO: Dr. OMalley reports personal fees, non-financial support and other from GSK/Tesaro; personal fees and other from AstraZeneca, Clovis, Tesaro, Abbvie, Amgen, Eisai, Merck, Agenus, GlaxoSmithKline, Regeneron, Genentech/Roche and Immunogen; personal fees from Ambry, Janssen/J&J, Myriad Genetics, Tarveda, and Novocure; and institutional funding from VentiRx, Array Biopharma, EMD Serono, Ergomed, Ajinomoto Inc, Ludwig Cancer Research, Stemcentrx, Inc, CERULEAN PHARMA, GOG Foundation, BMS, Serono Inc, TRACON Pharmaceuticals, Yale University, New Mexico Cancer Care Alliance, INC Research Inc., Inventiv Health Clinical, Iovance Biotherapeutics Inc., and PRA Intl.
LG: Dr. Gaba has nothing to disclose.
OWSY: Dr. Yap has nothing to disclose.
EG: Dr. Guerra reports consulting fees, advisory board fees, and travel support from Roche; consulting and advisory board fees from Clovis Oncology, Tesaro, PharmaMar, AstraZeneca, Merck Sharp & Dohme, and GlaxoSmithKline; and travel support from Baxter and GlaxoSmithKline/Tesaro.
PR: Dr. Rose has nothing to disclose.
J-FB: Dr. Baurain has nothing to disclose.
SG: Dr. Ghamande reports consulting at Seattle Genetics; speakers bureau at Tesaro/GlaxoSmithKline; and research funding from GlaxoSmithKline, Merck, Roche, Genentech, Takeda, Seattle Genetics, Advaxis, BMS, Clovis, Abbvie, and Tesaro.
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EP: Dr. Prendergast reports a consulting/advisory role at AstraZeneca and Merck.
CP: Dr. Pisano has nothing to disclose.
P: Dr. Follana has nothing to disclose.
KB: Dr. Baumann has nothing to disclose.
PMC: Dr. Calvert has nothing to disclose.
JK: Dr. Korach has nothing to disclose.
YL: Dr. Li is an employee of GlaxoSmithKline
DG: Dr. Gupta is an employee of GlaxoSmithKline.
BJM: Dr. Monk reports grants and personal fees from Tesaro.

**Sponsor:** GlaxoSmithKline, Waltham, MA, USA

**NCT number:** NCT02655016

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Efficacy of niraparib therapy in patients with newly diagnosed advanced ovarian cancer by BRCA and homologous recombination status: PRIMA/ENGOT-OV26/GOG-3012 study

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Objectives: Niraparib improves progression-free survival (PFS) in patients (pts) with newly diagnosed advanced ovarian cancer after first-line (1L) platinum-based chemotherapy (CT). We report the efficacy of niraparib in pts by biomarker status.

Methods: This double-blind, placebo (PBO)-controlled, phase 3 study randomized 733 pts with newly diagnosed advanced ovarian, primary peritoneal, or fallopian tube
cancer with a complete or partial response (CR or PR) to 1L platinum-based CT. Stratification factors were best response to the 1L CT (CR/PR), receipt of neoadjuvant CT (yes/no), and homologous recombination status (deficient/proficient/not determined). Pts received niraparib or PBO once daily. The primary endpoint of PFS assessed by blinded independent central review was analyzed using a stratified Cox proportional hazards model and hierarchically tested in homologous recombination deficient pts, then the overall population. Biomarker subgroup analysis of PFS was a prespecified exploratory analysis, and was performed using a stratified log-rank test and summarized using Kaplan-Meier methodology.

**Results:** Of 733 randomized pts (niraparib, 487; PBO, 246), 373 (51%) were homologous recombination deficient (niraparib, 247; PBO, 126) and 249 (34%) were homologous recombination proficient (niraparib, 169; PBO, 80). Overall, 35% had stage IV disease, 67% received neoadjuvant CT, and 31% had a PR to 1L CT. Niraparib-treated pts in all the biomarkers groups had a statistically significant and clinically meaningful benefit in PFS (Table). The most common grade ≥3 adverse events were anemia (31%), thrombocytopenia (29%), and neutropenia (13%).

**Conclusion:** Niraparib improved PFS as evidenced by reduction in the risk of recurrence or death due to any cause in the overall population of advanced ovarian cancer. No new safety signals were identified.

<table>
<thead>
<tr>
<th>Biomarker Subgroup</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.62 (0.502–0.755)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Homologous recombination deficient</td>
<td>0.43 (0.310–0.588)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BRCAmut</td>
<td>0.40 (0.265–0.618)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BRCAwt</td>
<td>0.50 (0.305–0.831)</td>
<td>0.0064</td>
</tr>
<tr>
<td>Homologous recombination proficient</td>
<td>0.68 (0.492–0.944)</td>
<td>0.0203</td>
</tr>
</tbody>
</table>

*mut=mutated, wt=wild type.*

**Disclosures:**

WLB: Dr. Bradley has nothing to disclose.

BJM: Dr. Monk reports grants and personal fees from Tesaro.

SH: Dr. Han has nothing to disclose.

BP: Dr. Pothuri reports grants, personal fees and non-financial support from Tesaro; and advisory board fees from AstraZeneca and Clovis Oncology.

MRM: Dr. Mirza reports personal fees and other from Karyopharm Therapeutics, Sera Prognostics; grants and personal fees from AstraZeneca, Clovis Oncology, Pfizer, Tesaro; personal fees from Genmed, BioCad, Soto, Geneos Therapeutics, Merck, Oncology Venture, Seattle Genetics, Sera Prognostics, Takeda Pharmaceutical Company Ltd, Zailab; and grants from Boehringer Ingelheim.

RB: Dr. Burger reports personal fees from Amgen, AstraZeneca, Tesaro, Clovis Oncology, Genentech, Gradalis, Janssen Research & Development, Merck, and VBL Therapeutics.

FH: Dr. Heitz reports non-financial support from NewOncology; personal fees from Roche, AstraZeneca, Clovis, Tesaro, and PharmaMar.

LVL: Dr. Van Le has nothing to disclose.
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CC: Dr. Churreca has nothing to disclose.
PD: Dr. DiSilvestro has nothing to disclose.
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J-FB: Dr. Baurain has nothing to disclose.
KJ: Dr. Jardon has nothing to disclose.
CP: Dr. Pisano has nothing to disclose.
PH: Dr Hoskins has nothing to disclose.
SH: Dr. Hietanen has nothing to disclose.
IM: Dr. Malinowska is an employee of GlaxoSmithKline
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AGM: Dr. González-Martín reports personal fees and non-financial support from AstraZeneca; grants, personal fees and non-financial support from Tesaro and Roche Holding AG; and personal fees from Clovis Oncology, Merck & Co. Inc., Genmab, Immunogen, PharmaMar S.A, and Oncoinvent AS.

**Sponsor:** GlaxoSmithKline, Waltham, MA, USA

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**Encore statement:** This data is presented on behalf of the original authors with their permission. Presented at Society of Gynecologic Oncology (SGO) annual meeting, March 28-31 in Toronto, Canada (abstract #31).
A quality improvement pathway to rapidly increase telemedicine services in a gynecologic oncology clinic during the COVID-19 pandemic

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IRB Review: The University of Wisconsin Institutional Review Board deemed this project exempt from review as a Quality Improvement project under 45 CFR 46.102(d)

Objective: We aimed to rapidly implement telemedicine in an outpatient Gynecologic Oncology (Gyn Onc) practice during the COVID-19 pandemic. The primary goal was to perform at least 50% of all outpatient clinical encounters using telemedicine within one week of implementation. The secondary goal was to analyze patient satisfaction with this transition.

Methods: The period from 3/16/2020 - 4/15/2020 was analyzed. The initial intervention involved transitioning asymptomatic cancer surveillance visits to telemedicine visits. A second intervention implemented after seven days, with RN and APP support, included transitioning postoperative and chemotherapy visits along with the distribution of a telemedicine note template. The Telehealth Satisfaction Survey (TSS) was administered to patients following their telemedicine visits.

Results: Within the four week study period, there were 409 outpatient encounters, 217 of which were telemedicine encounters (53.1%). During the week after the initial intervention and prior to the second, 1 out of 7 days (14.3%) reached the target threshold of 50% telemedicine encounters. Following the second intervention, 13 out of 15 days (86.7%) reached the target threshold of 50% telemedicine encounters. The TSS had a 75.3% response rate. Patients rated the following aspects of the telemedicine encounter as good or excellent: call quality (99.8%), personal comfort (93.8%), length of visit (97.3%), treatment explanation (96.4%), overall experience (90.2%). Additionally, 83% of patients would participate in a telemedicine encounter again.

Conclusions: It is feasible for a Gyn Onc outpatient clinic to rapidly implement systems to support telemedicine encounters. With interventions that included institutional IT support, multidisciplinary team planning, and standardized note templates, the goal of transitioning greater than 50% of outpatient encounters to telemedicine encounters was accomplished in the four week study period. Specifically, this goal was achieved on the majority of individual days after the implementation of the second intervention. Additionally, patients were overwhelmingly satisfied with the telemedicine encounters and the majority would participate in telemedicine encounters in the future.
Emotional health concerns of oncology physicians in the United States: fallout during the COVID-19 pandemic

Authors: Lauren Thomaier, MD1, Deanna Teoh, MD, MS1, Patricia Jewett, PhD2, Heather Beckwith, MD2, Helen Parsons, PhD3 Jianling Yuan, MD, PhD4 Anne H. Blaes, MD, MS2, Emil Lou, MD, PhD2, Jane Yuet Ching Hui, MD, MS5, Rachel I. Vogel, PhD1

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2University of Minnesota, Division of Hematology, Oncology and Transplantation, Minneapolis, MN  
3University of Minnesota, Division of Health Policy and Management, Minneapolis, MN  
4University of Minnesota, Department of Radiation Oncology, Minneapolis, MN  
5University of Minnesota, Department of Surgery, Minneapolis, MN

Introduction: Cancer care is significantly impacted by the Coronavirus Disease 2019 (COVID-19) pandemic. Our objective was to evaluate the effect of the pandemic on the emotional well-being of oncology providers across the United States and explore factors associated with anxiety and depression symptoms.

Methods and Materials: A cross-sectional survey was administered to United States cancer-care physicians recruited over a two-week period (3/27/2020 – 4/10/2020) using snowball-convenience sampling through social media. Symptoms of anxiety and depression were measured using the Patient Health Questionnaire (PHQ-4).

Results: Of 486 participants, 374 (77.0%) completed the PHQ-4: mean age 45.7±9.6 years; 63.2% female; all oncologic specialties were represented. The rates of anxiety and depression symptoms were 62.0% and 23.5%, respectively. Demographic factors associated with anxiety included female sex, younger age, and less time in clinical practice. Perception of inadequate PPE (68.6% vs. 57.4%, p=0.03) and practicing in a state with more COVID-19 cases (65.8% vs. 51.1%, p=0.01) were associated with anxiety symptoms. Factors significantly associated with both anxiety and depression included: degree to which COVID-19 has interfered with the ability to provide treatment to cancer patients and concern that patients will not receive the level of care needed for non-COVID-19 illness (all p-values <0.01).

Conclusion: The prevalence of anxiety and depression symptoms among oncology physicians in the United States during the COVID-19 pandemic is high. Our findings highlight factors associated with and sources of psychological distress to be addressed to protect the well-being of oncology physicians.
Clinical trial availability in gynecologic cancers compared to all cancer sites using mortality and incidence indices

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Objectives: To evaluate trends and differences of available clinical trials funded by public, industry, and other organizations (individuals, universities, and community-based) by comparing incidence and mortality indices.

Methods: Clinicaltrials.gov was queried for trials initiated from 2007-2016 for 18 cancer sites. The trials were categorized by funding sources and analyzed by the lethality of the cancer (years of life lost per new diagnosis) to generate standardized number of available studies to lethality (S/L) ratios. These were reported as studies funded by public (Sp/L), industry (Si/L), and other (So/L) organizations. To evaluate discrepancies in funding distribution, median Sp/L, Si/L, and So/L ratios of GYN cancers were compared to those of other cancers using Wilcoxon rank sum tests. Rates of change (ROC) among funding sources were calculated by linear regression with differences analyzed by two-tailed T-tests.

Results: While breast and prostate cancers are the 11th and 16th most lethal cancers respectively, breast (Sp/L 22.135, Si/L 30.797, So/L 32.429, Table 1) and prostate (Sp/L 21.232, Si/L 33.431, So/L 25.956) ratios were among the highest across funding sources. Ovarian cancer is the 5th most lethal with 10.8 years of life lost per new diagnosis but ranks 12th in median Sp/L (2.149 - lower than 10 other sites at p<0.05), 10th in Si/L (2.886 - lower than 10 other sites at p<0.05) and 14th in So/L (1.557 - lower than 12 other sites at p<0.05). Cervical cancer is 6th most lethal (8.7 years) with available S/L ratios of 15th (Sp/L=1.172), 16th (Si/L=0.691), and 15th (So/L=1.169). Over the ten year period, each GYN cancer showed a trend toward lower publicly-funded studies but rising industry- and other-funded trials per year. ROC of publicly-funded studies are significantly different from those of industry-funded trials for ovarian (p=0.023) and uterine (p=0.017) cancers.

Conclusions: Ovarian, cervical, and uterine cancers have significantly fewer funded studies when compared by lethality across funding categories. Within GYN cancers, there is a trend towards rising industry- and other-funded trials. This data can be used to investigate reasons for differential allocation of resources regarding clinical trial initiation from publicly-funded sources for GYN cancers.
Safety and efficacy of the anti–PD-1 monoclonal antibody dostarlimab in patients with recurrent or advanced dMMR endometrial cancer

Authors: Janet S. Rader1, Ana Oaknin,2 Anna V. Tinker,3 Lucy Gilbert,4 Vanessa Samouëlian,5 Cara Mathews,6 Jubilee Brown,7 Wei Guo,8 Hadi Danaee,8 Ellie Im,8 Renaud Sabatier9

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Objectives: Dostarlimab (TSR-042) is a humanized programmed death (PD)-1 receptor monoclonal antibody that blocks interaction with PD-1 ligands, PD-L1 and PD-L2. The objective of this interim analysis is to assess the safety and efficacy of dostarlimab in patients with mismatch repair deficient (dMMR) endometrial cancer (EC) who are enrolled in the GARNET trial (NCT02715284).

Methods: Patients with dMMR EC, as confirmed by immunohistochemistry, with recurrent or advanced disease that progressed on a platinum doublet regimen, were enrolled. Patients received 500 mg Q3W of dostarlimab for the first 4 cycles, then 1000 mg Q6W until disease progression or discontinuation. The primary endpoints were objective response rate (ORR) and duration of response (DOR), as assessed against Response Evaluation Criteria in Solid Tumors (RECIST v1.1) by blinded independent central review.

Results: As of the data cutoff, 104 patients with deficient mismatch mutation repair endometrial cancers were enrolled and dosed. Of these, 71 had measurable disease at baseline and ≥6 months of follow-up and were included in the efficacy analysis. The confirmed objective response rate was 42.3% (95% CI, 30.6%-54.6%); 12.7% of patients had a confirmed complete response, and 29.6% of patients had a confirmed partial response. Responses were durable; the median duration of response was not reached (median follow-up was 11.2 months). The estimated likelihood of maintaining response at 6 and 12 months was 96.4% and 76.8%, respectively. Anemia (2.9%), colitis (1.9%), and diarrhea (1.9%) were the most common grade ≥3 treatment-related adverse events. There were no deaths assessed as related to dostarlimab treatment.

Conclusions: Preliminary data for dostarlimab demonstrated clinical activity in patients with previously treated recurrent or advanced dMMR EC with an acceptable safety profile.
Disclosures:
JSR: Dr. Rader reports honoraria from AstraZeneca, Tesaro, GlaxoSmithKline, Roche Pharma, Clovis, and MSD; consulting or advisory role at AstraZeneca, Tesaro, GlaxoSmithKline, Roche Pharma, Clovis, MSD, Abbvie, Eisai, Immunogen, Takeda; research funding from Roche Diagnostics and Takeda; and travel, accommodations, and expenses from AstraZeneca, Roche Pharma, Clovis, and MSD.
AO: Dr. Oaknin reports consulting and Honoraria from AstraZeneca, Tesaro, Clovis, PharmaMar and Roche.
AVT: Dr. Tinker reports grants and personal fees from AstraZeneca.
LG: Dr. Gilbert reports personal fees from Merck, Astra Zeneca and Pfizer.
VS: Dr. Samouélian has nothing to disclose.
CM: Dr. Mathews reports institutional reimbursements from Tesaro.
JB: Dr. Brown reports honoraria fees from Olympus, consulting or advisory role fees from Caris, Tesaro, Clovis, AstraZeneca and Genentech; and speakers' bureau fees from Clovis outside the submitted work.
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HD: Dr. Danaee is an employee of GlaxoSmithKline.
EI: Dr. Im is an employee of GlaxoSmithKline.
RS: Dr. Sabatier reports grants from EISAI; personal fees and non-financial support from Roche and Pfizer; personal fees from Tesaro and Novartis; grants, personal fees and non-financial support from Astra-Zeneca; and non-financial support from Amgen.

Sponsor: GlaxoSmithKline, Waltham, MA, USA

NCT number: NCT02715284
Patient-reported outcomes (PRO) in the GARNET trial in patients (pts) with advanced or recurrent dMMR/MSI-H endometrial cancer (EC) treated with dostarlimab

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Objectives: PRO enable direct measurement of the experiences of patients with cancer. Anti-programmed death 1 (PD-1) therapies have shown favorable PRO in lung cancer but a data gap remains in EC.

Dostarlimab is an investigational anti-PD-1 monoclonal antibody which has shown promising activity in GARNET in advanced mismatch repair deficient (dMMR) EC pts (with an ORR of 42.3% and a disease control rate of 57.7%), and a low incidence of symptomatic grade ≥3 treatment-related adverse events (anemia [2·9%], colitis [1·9%], and diarrhea [1·9%]).

Here, we report on PRO measures collected from pts with dMMR/microsatellite instability high (MSI-H) EC in the single-arm GARNET trial.

Methods: Pts with dMMR/MSI-H EC confirmed by local tests, with recurrent or advanced disease that progressed on a platinum regimen were enrolled. Pts received 500 mg Q3W of dostarlimab for 4 cycles, then 1000 mg Q6W until disease progression or discontinuation. PRO assessment was an exploratory endpoint and was measured by the EORTC Quality of Life Questionnaire (QLQ-C30), a validated instrument used to evaluate quality of life, functioning, disease symptoms, and treatment-related side effects. PRO were collected at each dose administration, end of treatment, and follow-up. A mixed-model for repeated measures was used to assess change from baseline, accounting for time and baseline ECOG scores. The threshold to determine clinically meaningful group-level change was ±10 points.

Results: PRO data were available for 43 pts. Compliance rates were high at 98%. Relative to baseline, pts reported meaningful improvements in pain, insomnia, and social and emotional functioning over the trial duration. Appetite, nausea, vomiting, constipation, diarrhea, and physical and role functioning were stable over the trial duration. Quality of life and global health status were also maintained.

Conclusions: PRO from 43 pts enrolled in the GARNET trial show that disease- and treatment-related symptoms and quality of life are improved or maintained while
receiving treatment. These data, along with with the efficacy and safety profile of dostarlimab, support the use of dostarlimab in dMMR/MSI-H advanced EC.

Disclosures:
JSR: Dr. Rader reports honoraria from AstraZeneca, Tesaro, GlaxoSmithKline, Roche Pharma, Clovis, and MSD; consulting or advisory role at AstraZeneca, Tesaro, GlaxoSmithKline, Roche Pharma, Clovis, MSD, Abbvie, Eisai, Immunogen, Takeda; research funding from Roche Diagnostics and Takeda; and travel, accommodations, and expenses from AstraZeneca, Roche Pharma, Clovis, and MSD.
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JH: Dr. Huang is an employee of GlaxoSmithKline.
LE: Ms. Eliason is an employee of GlaxoSmithKline.
EI: Dr. Im is an employee of GlaxoSmithKline.
JB: Dr. Brown reports honoraria fees from Olympus; consulting or advisory role fees from Caris, Tesaro, Clovis, AstraZeneca and Genentech; and speakers' bureau fees from Clovis.

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The role of imaging in early detection of patients at risk for neuropathy during primary chemotherapy for ovarian carcinoma

Authors: Sarah G Bell, MD; Liam Dalton, BA; Brian Derstine, MS; Brian Ross; June Sullivan, MBA; Stewart Wang, MD, PhD; Shitanshu Uppal, MD, MBBS; Jean Siedel, DO

Objectives: Neuropathy is a common adverse event requiring dose reduction or regimen change in patients receiving platinum-taxane chemotherapy for ovarian cancer. Our aim was to determine whether specific biomarkers, such as skeletal muscle, visceral and subcutaneous fat cross-sectional areas, measured using computerized tomography (CT), were associated with the development of neuropathy. Morphomics has been used to predict oncologic outcomes with immunotherapy and to identify patients at higher risk for postoperative complications from major cancer surgeries. We hypothesized that patients who required dose reductions or regimen changes would have CT imaging findings that distinguished them from their counterparts who did not require dose reduction or regimen change.

Methods: All patients at our institution diagnosed with high-grade ovarian carcinoma between January 1, 2014 and December 31, 2018 were identified retrospectively. Analytic Morphomics, a semiautomated image analysis method, was used to extract measures of body composition from CT images at the level of the third lumbar vertebra. Demographic and clinical characteristics were abstracted from the electronic medical record. We analyzed several binary outcomes (neuropathy, delay in chemotherapy, or dose reduction by cycle 1, 3 or 6) and used unpaired, two-tailed t-tests to compare means between each outcome group at each timepoint.

Results: Of 156 patients screened for the study, 138 patients were included and had pre-treatment CT scans available and completed six cycles of platinum-taxane chemotherapy. Patients who developed neuropathy in any of the six cycles, or had a change in their chemotherapy regimen by cycle six, had higher mean visceral fat area (VFA) than those who did not develop neuropathy. This finding was statistically significant throughout three cycles (p=0.023) and six cycles (p=0.030).

Conclusions: Increased visceral fat on CT imaging was significantly associated with a higher incidence of neuropathy and change in chemotherapy regimen in patients undergoing primary platinum-taxane chemotherapy for ovarian carcinoma. Weight and BMI did not have a significant association with development of neuropathy, dose reduction, or treatment delay. Further study is needed to determine if dose reductions or regimen changes due to neuropathy can be better predicted using morphomics.
Missed opportunities for HPV vaccination at academic outpatient gynecology clinics in a Midwest metropolitan area

Authors: Devin E. Jones MD, Tavonna D Kako MD, Surya Bhamidipalli, Monica K. Neuman MD, Luisa L. Vera MD, Caroline E. Rouse MD, Sharon E. Robertson MD, MPH

Objective: HPV vaccination rates are low and HPV-associated malignancies are on the rise. Here, we analyze the rate of missed opportunities for HPV vaccination for eligible women at academic outpatient gynecology clinics in a Midwest metropolitan area.

Methods: We performed a retrospective chart review of vaccine-eligible patients, 26 years of age and younger, who presented to one of ten gynecologic clinics affiliated with an academic medical center in the Midwest between October 1, 2016 and October 1st, 2019. A missed opportunity for vaccination was defined as those patients who were eligible for HPV vaccination, had no documentation of previous vaccination, and for whom an HPV vaccination was not offered at the gynecologic visit. Pregnant and postpartum patients were excluded. Descriptive statistics were performed to summarize demographic and visit specific data and a multivariate analysis to determine factors associated with missed opportunity for vaccination is ongoing.

Results: A total of 3,283 vaccine-eligible women ages 26 years and younger attended gynecology visits during the study time period. The majority of women were non-white (84%) and 32% identified Hispanic ethnicity. Seventy-seven percent of all eligible visits were paid for by a public insurer or self-pay. In this population, a total of 1,270 women (39%) had received at least one dose of the HPV vaccine in their lifetime. For those women offered vaccination at their visit, less than 6% declined the vaccine.

Conclusions: More than half of gynecologic visits for vaccine eligible women at these clinics qualified as a missed opportunity. Historically, the burden of HPV vaccination has fallen to our pediatric and primary care colleagues. However, the outpatient gynecology clinic visit provides a unique opportunity to address HPV vaccination in those women that were not vaccinated at the recommended age. With the recent FDA expansion of the vaccine-eligible age range up to 45 years, gynecologists now have an even larger population of potentially at-risk patients who may be eligible for vaccination.
The association of risk perception, response efficacy and HPV vaccine decision making among adolescent parents/guardians

Authors: Alicia Myhre, DO, MS, Tiaj Xiong, Rachel I Vogel, PhD, Deanna Teoh, MD, MS

Objective: To evaluate the association of risk perception and response efficacy (belief a behavior will result in the intended outcome) among parents/guardians with adolescent HPV vaccination decisions.

Methods: A cross-sectional survey of adolescent parents/guardians was conducted over a 1-week period at the Minnesota State Fair. To measure risk perception, participants ranked HPV and vaccine risks against diseases/side-effects for which numerical risks were provided. To measure response efficacy, participants indicated (scale 0-100) their ability to prevent HPV infection. Chi-squared and Fisher’s exact tests compared risk perception and response efficacy of those who vaccinated/planned to vaccinate against HPV (“vaccinators”) with those with no plan to vaccinate (“non-vaccinators”).

Results: Of 405 participants, 74% were vaccinators, 13% were non-vaccinators. Non-vaccinators were more likely to under-estimate risk of HPV-related cancers (p<0.05) and over-estimate risk of vaccine-related side-effects (p<0.05); perceived risk of genital warts did not differ by vaccination decision (p=0.5). Non-vaccinators were more confident in their ability to prevent HPV infection without vaccination (mean score 64.1±23.9 vs. 30.0±29.2; p<0.0001), less confident in their ability to prevent HPV infection with vaccination (51.7±30.5 vs. 74.8±25.5; p<0.0001). The primary healthcare information source for non-vaccinators was more likely to be online (16% vs. 4%), and less likely to be a healthcare provider (53% vs. 87%; p<0.0001).

Conclusions: Low HPV risk perception and high response efficacy of non-vaccination HPV prevention behaviors are associated with the decision not to vaccinate. Multi-modal education about HPV prevention is needed, as non-vaccinators are also less likely to get healthcare information from a healthcare provider.
Changes in positive predictive value of cervical cytology following HPV vaccination

Authors: Gwiwon Nam, Rachel I. Vogel, PhD, Shalini Kulasingam, PhD, Deanna GK Teoh, MD, MS

Objective: Minnesota HPV vaccination initiation and completion rates are similar to the national average. Statistics predict that as dysplasia prevalence decreases, positive predictive value (PPV) of cervical cytology will also decrease. The objective of this study was to examine if current U.S. HPV vaccination coverage has decreased dysplasia prevalence enough to diminish the positive predictive value (PPV) of abnormal cervical cytology using a Minnesota sample.

Methods: This retrospective cohort study comprised a chart review of all patients 21-35 years of age who had at least 1 Pap test result within MHealth/Fairview 2016-2018. HPV vaccination data, cervical cancer screening data and dysplasia results were extracted. Vaccinated was defined as receiving at least 1 dose of HPV vaccine, with subgroup analyses performed for those completing vaccination per ACIP guidelines and by age of initiation dichotomized as 21+ years versus <21 years.

Results: 49,764 patients meeting study criteria were identified. Among the entire study population, 10% had abnormal cytology results during the study period. Among the 4,928 patients with abnormal cytology, PPV for CIN2+ was lower among vaccinated individuals (13% vs.18%; p<0.0001) than among non-vaccinated individuals. Among vaccinated individuals, PPV was lower among those completing vaccination (12% vs. 16% for incomplete vaccination; p=0.04). In addition, PPV was lower among initiating vaccination at <21 years of age (9% vs 26% for 21+y; p<0.0001).

Conclusions: Among a population with low HPV vaccine coverage, the decrease in dysplasia prevalence among vaccinated individuals is resulting in a subsequent decrease in PPV of cervical cytology, particularly in those initiating vaccination prior to 21 years of age and among those completing the series. Confirmation of these results will call for changes in screening strategies for vaccinated individuals.
Postpartum tubal sterilization practice patterns following recommendations for opportunistic salpingectomies in lieu of tubal ligation

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Background: Tubal ligation is the most common form of contraception utilized by women in the United States. Salpingectomy can be considered an alternative to tubal ligation both for contraception and potential ovarian cancer risk reduction. In November of 2013, the Society of Gynecologic Oncology (SGO) released a recommendation to offer salpingectomy at the time of pelvic surgery for ovarian cancer risk reduction. Our objective was to determine the proportion of immediate postpartum sterilization procedures completed as bilateral salpingectomies (BS) between 2009-2019, and analyze practice patterns as they changed following the SGO statement.

Methods: An IRB approved retrospective cohort study was conducted at a single academic hospital between January 2009 and December of 2019. All patients undergoing postpartum tubal sterilization within 48 hours of vaginal delivery were included. Patient demographics, peripartum and perioperative data was collected and analyzed. The primary outcome was the proportion of sterilizations completed as bilateral salpingectomies before and after 2014.

Results: 317 women underwent postpartum sterilization between 2009-2019. Median age and BMI were 32 and 31.4 respectively. 113 patients underwent BS (36%). All bilateral salpingectomies were performed in 2014 or later. In 2014, 6% of patients receiving postpartum tubal sterilization underwent BS compared to other forms of tubal sterilization; this progressed to 80% of patients in 2019. All patients with a family history of BRCA underwent BS (n=4, p=0.007). Patients were more likely to receive opioids at discharge between 2013 and 2017 (OR 3.86 CI 2.62-5.67) and Hispanic patients were less likely than white patients to receive opioids at discharge (OR 0.37 CI 0.2-0.67). Patients insured by Medicaid were significantly less likely to receive bilateral salpingectomy (OR 0.43, CI 0.25-0.73), controlling for other factors.

Conclusions: Practice patterns for postpartum BS are changing and do not appear to be influence by prohibitive patient factors such as BMI and a history of pelvic surgery. Postoperative complications have remained stable since the induction of postpartum BS. Patients insured by Medicaid are less likely to receive risk reducing BS following vaginal delivery – highlighting a previously unknown disparity.
65 Revisited: A Revised Markov Model for Evaluating Oophorectomy at the Time of Hysterectomy for Benign Disease

Authors: Shannon K Rush, MD; Xiuyu Ma, PhD candidate; Michael A. Newton, PhD; Stephen L. Rose, MD

Objectives: Decision to perform oophorectomy at the time of benign hysterectomy must balance risks of cardiovascular disease (CVD), breast and ovarian cancers, and re-operation. A Markov model published in 2005 argued against performing oophorectomy in women even up to age 65, but we found inconsistencies in the data utilized. We sought to revisit that model with updated data and corrected statistical modeling.

Methods: We performed a literature review assessing hazard ratios (HRs) for mortality by disease, age, hysterectomy (HYS) with or without bilateral salpingo-oophorectomy (BSO), and hormone replacement therapy (HRT) use. Base mortality rates were derived from National Vital Statistics. A Markov model from reported hazard ratios predicted proportion alive to age 80 by 5 year age groups at time of surgery. Model-based computations were performed with R, version 3.5.1. We accommodated HR uncertainty using Bayesian integration.

Results: Performing BSO before age 50, without HRT use, yields lower survival proportion to age 80 (62.7% alive to 80 with HYS vs 58.9% with BSO, p<0.001). After age 50, there were similar proportions living to age 80 with HYS alone vs concurrent BSO (64.8% vs 64.8%, p=0.92). Importantly, those taking HRT after BSO before age 50 had similar proportions of CVD, stroke, and alive to 80 as those undergoing BSO after age 50 or HYS alone.

Conclusions: This updated Markov decision model argues for considering concurrent BSO for woman greater than age 50. It allows providers to counsel women who have oophorectomy before age 50 to initiate HRT to mitigate increased mortality risk.

Table 1. Mean Survival to age 80 when comparing Age at Surgery and use of Estrogen Replacement Therapy after Surgery.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Estrogen use</th>
<th>Age at surgery</th>
<th>Mean survival to age 80</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYS</td>
<td>No</td>
<td>Before 50</td>
<td>62.7%</td>
</tr>
<tr>
<td>BSO</td>
<td>No</td>
<td>Before 50</td>
<td>58.9%</td>
</tr>
<tr>
<td>HYS</td>
<td>No</td>
<td>50 - 60</td>
<td>64.8%</td>
</tr>
<tr>
<td>BSO</td>
<td>No</td>
<td>50 - 60</td>
<td>64.8%</td>
</tr>
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<td>HYS</td>
<td>Yes</td>
<td>Before 50</td>
<td>62.7%</td>
</tr>
<tr>
<td>BSO</td>
<td>Yes</td>
<td>Before 50</td>
<td>62.7%</td>
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</tbody>
</table>

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