Abstracts

Presenting Residents

Characteristics of adolescents with CIN 3: findings from a tertiary care colposcopy database

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Objective: To identify demographic characteristics of adolescents with high grade histology

Methods: Our review of the literature identified several risk factors for high grade lesions including number of lifetime sexual partners, history of sexually transmitted infections, parity, HIV status, smoking, ethnicity and low socio-economic status. At our hospital, demographic characteristics, medical history, cytologic diagnosis and histologic diagnosis of women referred to our colposcopy clinic have been collected in a database. Using our institutional colposcopy database, we identified 841 adolescents (defined as ≤20 years of age) seen for the evaluation of an abnormal Papanicolaou smear between January 1st, 1999 and September 30, 2007. For the purposes of this analysis, we excluded 197 young women without available histologic results and 30 who did not have number of partners recorded. Our hypothesis was that teens with 4 or more lifetime sexual partners are twice as likely to have CIN3 or higher as compared to teens with 3 or fewer partners. Our secondary outcomes were to investigate the other aforementioned demographics. Unconditional multivariable logistic regression was used to calculate odds ratios and 95% confidence intervals for patient characteristics and the detection of CIN3+. Characteristics associated with CIN3+ with p<=0.1 in the crude analysis were added to a multivariable regression model. Data analysis was performed with SAS version 9.1.

Results: Of the 614 eligible adolescents, the median age was 19, with a range of 13-20. The population was largely nulliparous, single (579 or 95%), not privately insured (455 or 82%), and racially/ethnically diverse (198 or 33% Hispanic, 246 or 42% non-Hispanic white and 108 or 18% non-Hispanic black). Only one was HIV positive. The mean age at first intercourse of the cohort was 15.3 years (SD 1.7), and the median number of lifetime male sexual partners was 4 (range 1-50). Mild cytologic abnormalities predominated, with 329 adolescents (53%) referred to colposcopy for LSIL and 184 (30%) for ASC-US. HSIL was documented in 64 (10%) of the population. Clinically significant histologic disease (CIN 3+) was found in 54 (8.8%). No cases of invasive disease or AIS were found. In our univariate analysis, gravidity, parity, marital status, insurance status, race/ethnicity, smoking, age at first coitus, lifetime male sexual partners and pregnancy were not associated with increased odds of CIN3. History of sexually transmitted infections and indication for colposcopy, as expected, were.

Conclusion: In this study population of over 600 young women with an initial cytologic abnormality, the prevalence of CIN 3 was 8.8%. Risk factors in the adult population for dysplasia such as number of sexual partners, parity, smoking, ethnicity and low socio-economic status (as measured by insurance status) were not risk factors in this adolescent population for CIN3. History of sexually transmitted infections and indication for colposcopy did have increased odds of CIN3. Our multivariate analysis confirmed these findings, both including and excluding the variable of number of partners.

Intrapartum group B streptococcus prophylaxis in patients who report a penicillin allergy: Has there been an improvement in adherence to the 2002 CDC guidelines?

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Objective: To compare adherence to the 2002 CDC guidelines for the prevention of perinatal group B streptococci (GBS) disease in penicillin allergic patients between 2004-2006 and 2008.

Methods: In 2007, we conducted a retrospective cohort study of all GBS-positive, penicillin-allergic women who delivered at Women and Infants Hospital (WIH) between 2004 and 2006 (n=233). Because
this study demonstrated suboptimal adherence to the 2002 CDC guidelines, WIH conducted a series of hospital based interventions to improve adherence. To determine whether or not adherence improved, we repeated this study with a retrospective cohort of GBS positive, penicillin allergic patients who delivered at WIH between April 2008 and January 2009 (n=74). Medical records were analyzed. Main outcome measures were (#1) the proportion of penicillin-allergic, GBS positive patients who had antimicrobial sensitivity testing performed and (#2) the proportion of penicillin-allergic, GBS positive patients who received the appropriate antibiotic based on 2002 CDC guidelines. Women with either a scheduled cesarean delivery or a preterm delivery were excluded from analyses. We compared main outcomes between this 2008 dataset and the 2004-2006 dataset. Based on number of eligible cases identified for analyses and assuming $\alpha$=0.05, we had approximately 95% power to detect a 25% difference in both proportion with antimicrobial sensitivity and proportion with appropriate antibiotic received. Data were analyzed using STATA 9.0.

Results: In 2008, 94.2% (95% confidence interval [CI]= 87-97%) of GBS-positive, penicillin-allergic women received antibiotic prophylaxis (n=98) and 76.2% (95% CI 66-84%) of GBS pos, penicillin-allergic women received appropriate antibiotics (compared to 16.2% in 2004-2006, p<0.001). Antimicrobial sensitivity testing was performed in 79.4% of cases (95% CI 68-87%), compared to 11.4% in 2004-2006 (p=0.001). Among patients who did not have antimicrobial sensitivity testing, 50% received clindamycin (n=7) and 42% received vancomycin (n=6). Among cases where an appropriate antibiotic was not administered 80% received clindamycin (n=11).

Conclusion: Adherence to the 2002 CDC guidelines for GBS prophylaxis in penicillin-allergic women has increased dramatically since the 2004-2006 data collection period. However, there is continued room for improvement and efforts aimed to optimize adherence should be implemented and maintained.

Long-term use of pegylated liposomal doxorubicin in recurrent ovarian carcinoma

Author: Beth Cronin, MD
Preceptors: Don S. Dizon, MD & Katina Robison, MD

Objective: Ovarian cancer is the fifth leading cause of death in women, with an estimated five-year survival of thirty percent. For women who relapse, pegylated liposomal doxorubicin (PLD) is a FDA-approved agent for the treatment of recurrent disease, with response rates ranging from 16 to 20. However, there is no consensus on whether treatment should be to progression or to best response, and very little is known about the outcomes of women receiving PLD beyond six cycles. The aim of this project is to determine progression free survival of this highly selected population, as compared to women who received only six cycles.

Methods: A retrospective chart review was performed of women receiving 6 or more cycles of pegylated liposomal doxorubicin between 1998 and 2007. All patients with recurrent ovarian, fallopian tube, primary peritoneal, or uterine papillary serous carcinoma were included. Those who received only 6 cycles were our control group. Evaluation for progression was based on CA-125, physical examination, and imaging studies.

Results: Forty eight patients were included in our analysis: 36 (75%) received a median of 9 cycles of PLD (range 7 to 28) and 12 (25%) received 6 cycles who made up the control group. The median PFS were 11 (range 6-29) and 8.5 months (range 6-15). The difference between these two groups was not statistically significant (p=0.065). Of the 36 patients receiving over 6 months of treatment, 25 (69%) were treated less than one year and the remaining 11 (31%) received 12 months or more of treatment. Comparing these two groups, the median PFS was 8 (range 6-29) and 16 months (range 14-28 months), which was a statistically significant difference (p<0.001).

Conclusion: In this highly selected population, no difference in PFS was seen in women treated with PLD by duration of therapy. However, for the group able to remain on therapy for 12 months or longer, PFS was significantly longer than those women who received it for less time. This suggests that PLD may be used to treat until progression and for those able to stay on it, may prove effective in prolonging PFS.

Increased interpersonal partner violence inquiry with standardized health prevention screening
Objective: To evaluate the impact of patient and provider variables on rates of intimate partner violence screening in an ambulatory gynecology practice.

Methods: A cross-sectional study of 300 patients chosen randomly from annual healthcare visits during 2007 at a university-affiliated ambulatory gynecology clinic. All encounters were recorded on a standardized health history form which included questions about abuse history. Data on patient and provider characteristics were collected. The association of provider screening with selected patient variables was assessed using multivariable logistic regression.

Results: The median age of the study population was 29 (range 15-73). In general, the cohort was racially/ethnically diverse and the majority was on government assistance. Sixty-seven percent (194/291) had children living at home, and 57% (164/286) were single. Of the 300 patients, 243 (81%) had documentation of abuse screening in their medical records. Variables previously found to be associated with higher rates of partner abuse, such as younger age, increased parity, or substance abuse, did not influence whether patients were screened. Similarly, differences in screening by provider type (NP/resident) or gender did not emerge. Patients were, however, significantly more likely to be questioned about partner violence when they received other preventive screening (adjusted OR 2.50 (1.26-4.99)) or presented with a somatic pain complaint (adjusted OR 2.55 (1.12-5.83).

Conclusion: Ambulatory gynecology patients were more likely to be screened for intimate partner violence when providers performed other preventive health screening utilizing a standardized health history form.

Effect of routine pelvic floor exercise counseling and pelvic floor physical therapy on symptoms and life impact for female pelvic floor disorders

Objective: Our primary objective was to evaluate the effect of pelvic floor physical therapy (PFPT) compared to routine pelvic floor education on symptoms and life impact in women with pelvic floor disorders (PFD). Our secondary objective was to evaluate the combined effect of both PFPT and routine education on improving symptoms and life impact of PFDs.

Methods: This is a prospective cohort study of women with PFDs who opted for treatment with PFPT. All women received routine education on pelvic floor exercises from physicians, then enrolled and completed a course of PFPT. Patients completed PFD-specific questionnaires for symptom bother [Pelvic Floor Distress Inventory-20 (PFDI-20)] and life impact [Pelvic Floor Impact Questionnaire-7 (PFIQ-7)] at the following time points: 1) prior to any intervention; 2) after routine education and performing independent pelvic floor exercises; and 3) after completing PFPT. Women also completed the Sexual Function Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) and Body Image Scale (BIS) before and after completing PFPT. Paired t-tests and a one sample binomial test were performed to measure improvement in scores.

Results: Thirty four participants have been enrolled and recruitment is ongoing. Twenty-three participants have completed the study and are included in this analysis. The mean age of study participants was 57.8 years. The majority of the women are Caucasian (95.7%), menopausal (73.9%), nonsmokers (95.7%), with a median parity of 2. Thirty percent reported prolapse symptoms, 34.8% reported defecatory symptoms, and 72% reported urinary incontinence symptoms at baseline. The median number of PFPT sessions was 4, with a mean duration of 6 weeks. For our primary objective comparing routine education vs PFPT, there were no differences in symptom bother, life impact, sexual function, or body image between groups in this preliminary analysis. For our secondary objective, women reported significant improvement in PFD symptom bother (mean PFDI score 101 ± 54 vs 62 ±38, p=.04 for baseline versus post PFPT, respectively) and life impact (mean PFIQ score 50 ± 44 vs 23 ± 27,
Repeat teen birth: does mode of delivery make a difference?

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**Objective:** To evaluate the association between repeat teen births and mode of delivery (cesarean vs. vaginal) in adolescent mothers.

**Methods:** Vital statistics data from the Rhode Island Department of Health for the years 2004-2006 were used to conduct this retrospective cohort study. The 2004 vital statistics records were searched for all singleton first births to mothers 19 years old and younger. Birth files for the years 2005 and 2006 were searched to match those adolescents having a subsequent live birth within 24 months of the index birth. Maternal baseline characteristics and infant birth record data for each birth were collected. Repeat birth rates were calculated and compared between adolescents delivering their first baby via cesarean vs. vaginally. Fisher’s exact test, Wilcoxon rank sum test, and survival analysis methods were utilized.

**Results:** 899 adolescents delivered their first child in 2004. 18.6% (n=167) delivered via cesarean and 81.4% (n=732) delivered vaginally. Overall, the repeat birth rate within two years was 15.9% (n=143) with 17.4% for cesarean delivery and 15.6% for vaginal delivery. Median time to repeat birth in the cesarean cohort was 20 months and in the vaginal cohort was 17.6 months. The cohorts differed statistically (p-value <0.01) with regard to pregnancy complications (72.5% for cesarean vs. 17.8% for vaginal) and birth weight (3347g for cesarean vs. 3197g for vaginal). A time-to-event analysis (time-to-next-delivery) showed differences in the rates of repeat pregnancy over time. 15-20 months after the first birth, the vaginal cohort had a higher rate of repeat births; and 21-24 months after the first birth, the cesarean cohort had a higher rate.

**Conclusion:** We observed a slightly higher rate of repeat birth within two years of an index birth for teen mothers whose first birth was by c-section compared with vaginal delivery; this difference was not statistically significant. The trend in time-to-next-delivery may give the most information about when to direct interventions, reinforce contraceptive messages and provide education around pregnancy prevention and planning for parenting teens.

Comparison of a novel multiple biomarker assay to the risk of malignancy index for the prediction of epithelial ovarian cancer in patients with a pelvic mass

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**Objective:** Patients with epithelial ovarian cancer (EOC) have decreased morbidity and increased survival when initially cared for by gynecologic oncologist at centers experienced in the management of EOC. Therefore, it is important to be able to triage patients at increased risk for EOC to the appropriate centers. The objective of this trial is to compare the risk of malignancy index (RMI) to the Risk of Ovarian Malignancy Algorithm (ROMA), a novel multiple marker assay for the prediction of EOC in patients with a pelvic mass.

**Methods:** Multicenter prospective trial. All patients had a documented pelvic mass on imaging and had preoperatively determined serum values for HE4 and CA125. Surgical pathology results were confirmed.
through a central review. An RMI and ROMA were determined for each patient. Sensitivity and specificity were calculated for each method and compared.

**Results:** 566 patients enrolled into the trial with 456 evaluable patients. There were 123 EOC (17 stage I, 17 stage II, 80 stage III, 6 stage IV and 3 unstaged), 22 LMP, and 311 benign tumors. There were 175 premenopausal patients and 281 postmenopausal patients. Examination of all patients and stages at a set specificity of 75% revealed ROMA had a sensitivity of 95% (95% CI: 90-98) and the RMI had a sensitivity of 84% (95% CI: 76-90) for determining benign from EOC. In patients with stage I and II disease, the ROMA achieved a sensitivity of 88% (95% CI: 73-97) compared with the RMI sensitivity of 62% (95% CI: 44-78). For patients with stage I, II, IIIA/B and node positive only IIIC, the ROMA had a sensitivity of 91% (95% CI: 50-80) and the RMI had a sensitivity of 66% (95% CI: 44-78). The sensitivity for stage III and IV patients with bulky disease was 99% (95% CI: 93-100) for ROMA and 95% (95% CI: 87-99) for RMI.

**Conclusion:** The dual marker algorithm utilizing HE4 and CA125 to calculate a risk of malignancy achieves a greater sensitivity for the detection of EOC. The ROMA accurately stratified patients with early stage I & II, stage IIIA and IIIB disease into the high risk group.

### Presenting Fellows

**The role of transforming growth factor β in cervical remodeling within the rat cervix**

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**Objective:** Transforming growth factor β, (TGFβ) plays a central role in extracellular matrix (ECM) remodeling. We hypothesized that TGFβ signaling is involved in this process. This study evaluates patterns within this signaling pathway.

**Methods:** The cervix of non pregnant and timed pregnant rats were obtained. mRNA expression of TGFβ1, TGFβ-Receptor 1 (TβR1), TβR2, and TβR3 was evaluated. Four animals were sacrificed for each time point. Western blotting was performed for protein expression. Smad2 and 3 phosphorylation were assessed to evaluate TGFβ activation.

**Results:** TGFβ1 mRNA increased through day 21 and declined on day 22 (ANOVA p=0.001). TβR1 expression was unchanged. TBR2 and TβR3 mRNA expression was similar to TGFβ1. TβR3 protein expression was similar to mRNA. Smad2 phosphorylation paralleled changes in TβR3.

**Conclusion:** Components of the TGFβ signaling pathway increase during pregnancy along with Smad2 activation. The decline on day 22 correlates with a transition to the ripening phase supporting a role in cervical remodeling.

**The association between stage II posterior prolapse and obstructive bowel symptoms**

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**Objective:** The primary objective of this study is to estimate the association between stage II posterior prolapse and obstructive bowel symptoms.

**Methods:** This is a secondary analysis of a cross-sectional study of all women presenting for initial visit at a tertiary center for pelvic floor disorder. Each woman was asked to complete the short forms of the Pelvic Floor Distress Inventory-20 (PFDI-20) and the Pelvic Floor Impact Questionnaire-7 (PFIQ-7). Exposure was defined as stage II posterior vaginal prolapse or greater as measured by POP-Q measurements. Outcomes included the separate bothersome obstructive bowel symptoms defined as a response of moderately bothered (3) or quite a bit of bother (4) to items #4, 7, or 8 (splinting, straining, or
incomplete bowel emptying, respectively) on the PFDI-20. A secondary outcome was a composite of all three bothersome obstructive bowel symptoms. Multiple logistic regression models were constructed to estimate the effect of stage II posterior prolapse or greater on the odds of each individual bothersome bowel symptom and of a composite of all three symptoms. Potential confounders identified on univariate analysis (p <.1) were included in the final models.

**Results:** Our study included 721 women. Mean BMI was 28.8 (±6.6) and mean age was 56.6 (±16.2). Stage II posterior prolapse or greater was present in 233 (32.3%) women. Individual symptoms of bothersome splinting, straining, and incomplete bowel evacuation were reported by 118 (16.4%), 150 (20.8%), and 144 (20.0%), respectively. Univariate analysis did not show an association between stage II posterior prolapse or greater and the separate symptoms of straining or incomplete bowel emptying. Univariate analysis did show an association between stage II posterior prolapse or greater and the individual symptom of splinting (Crude OR 2.08; 95%CI 1.39, 3.12) and the composite bothersome obstructive bowel symptoms (Crude OR 1.4; 95%CI 1.02, 1.97). However, on multiple logistic regression, stage II posterior prolapse or greater was not associated with an increased odds of composite obstructive bowel symptoms (Adjusted OR 1.30; 95%CI .92, 1.83) after adjusting for potential confounders of menopausal status, vaginal parity, prior hysterectomy, prior urinary incontinence procedure, and irritable bowel syndrome. Bothersome splinting was associated with stage II posterior prolapse or greater (Adjusted OR 1.92; 95%CI 1.27, 2.90) after adjusting for potential confounders of age, menopausal status, and prior hysterectomy.

**Conclusion:** The symptom of bothersome splinting was associated with stage II posterior prolapse or greater, but the bothersome bowel symptoms of straining and sensation of incomplete bowel evacuation were not.

**Accuracy of office-based ultrasound guided needle biopsies performed by a dedicated breast surgeon**

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**Objective:** Studies have shown that ultrasound-guided core biopsies (USGCB) are accurate and cost effective at diagnosing breast disease compared to excisional biopsy. There has been recent debate as to whether surgeons are qualified to perform image guided biopsies, typically performed by radiologists. The purpose of this study is to determine the accuracy of USGCB performed by breast surgeons at the Breast Health Center of an academic women’s oncology program.

**Methods:** Following IRB approval, we identified 100 patients who underwent an USGCB by a breast surgeon as part of their diagnostic work-up from 1/2003 to 8/2008. Data collected included patient age, date of presentation, clinical and radiologic findings, date of biopsy and subsequent surgery, type of biopsy technique used, laterality, number of biopsies performed and pathology from both biopsy and final excision.

**Results:** Of the 100 patients seen at the Breast Health Center, 72 (72%) presented with a palpable breast mass, 12 (12%) presented with an abnormal mammogram. The mean age at presentation was 43.4 years (range, 16-80). Of these, 89% had a formal radiologic US (FRU), and 56% underwent definitive excision. Eighty patients underwent USGCB at the time of initial consultation (80%). Comparing clinical impression of benign vs. malignant disease derived from office based US (OBU) to FU, there was 98.11% agreement (Kappa statistic: 0.96 (SE: 0.14), p<0.0001). There was good agreement on maximal dimensions between OBU and FRU (Spearman correlation of 0.75, p<0.0001). Compared to final pathology at excision, office based UGCB showed 50% agreement. However, when classified as benign versus malignant there was 96.4% agreement (95%CI: 87.7-99.6%). The average time from biopsy to surgery in 56/100 patients was 61.4 days.

**Conclusion:** USGCB of the breast performed in the office setting by dedicated breast surgeons are highly accurate at diagnosing both benign and malignant lesions. The majority of patients seen in the surgeon’s
office undergo an U/S guided procedure at the time of initial consultation allowing early diagnosis and treatment of breast disease. The comparative accuracy of an OBU vs. FU biopsy requires further study.

Human artificial ovary by pre-fabricated cellular self-assembly
Author: Stephan Krotz, MD
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Objective: Culturing ovarian tissue for in vitro human oocyte maturation and maturation of human primordial oocytes has met with limited success. Previous attempts suggest that theca-granulosa cell interaction may be instrumental. We present the first 3-dimensional co-culture of human cumulus-oocyte complexes and theca cells in a prefabricated assembly of a model artificial human ovary.

Methods: Theca cells were isolated from the follicles of reproductive age patients mechanically under a dissection microscope and by digestion with 0.5% collagenase. They were cultured in DMEM with 10% FBS and antibiotics in 3-dimensional nonadhesive agarose hydrogel molds forming spheroids, toroids and honeycomb-like blocks. Growth, compaction, and macrostructural behaviors were assessed daily for one week on all structural types. Immunohistochemistry staining with anti-calretinin confirmed theca cell identity and live-dead staining was performed at the end of one week to confirm cellular viability. Cumulus-oocyte complexes were harvested from the antral follicles of oophorectomy specimens from reproductive age women. The cumulus-oocyte complexes were placed into the openings of theca cell honeycombs after 18 hours of co-culture. The resulting co-culture model was further cultured for 48 hours.

Results: Theca cells were isolated and cultured with simple growth media. Complex three dimensional structures such as the honeycomb can be formed with theca cells, harvested from their respective molds and remain viable for at least seven days. This artificial ovarian construct maintains its 3-dimensional structure on flat agar-coated dishes for greater than 48 hours. Contact between the theca cell honeycomb and the granulosa cell spheroids occurs with maintenance of their respective forms. The ability of these self-assembled structures to maintain form is consistent with previous findings from our laboratory. This is the first time, however, that we demonstrate absence of stromal invasion into a second cell type.

Conclusion: Human theca and granulosa cells isolated from ovarian tissue can be induced to form complex 3-dimensional structures through self-assembly. These self-assembled structures can be co-cultured to create an artificial ovary for in vitro oocyte maturation and serve as a model for human ovarian development and toxicology studies.

The use of a vitamin D derivative in a mouse xenograft ovarian cancer model.
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Objective: Epithelial ovarian cancer (EOC) is the leading cause of death from gynecologic malignancies in the United States. The vast majority will succumb to their disease because of drug resistance to standard agents, most notably platinum analogs. As a result, there is a critical need to develop new drugs for EOC that will expand the options beyond platinum-based treatment. Our laboratory has been interested in vitamin D derivatives (VDDs) as potential anti-solid tumor drugs. We performed in vitro studies with SKOV-3 ovarian cancer cells treated with ergocalciferol-derivative (MT19C), which demonstrated it is a potent and selective inhibitor of ovarian cancer cells. Based on these findings, we hypothesized that MT19C exerts cytotoxic effects on EOC while not causing hypercalcemia. We developed a mouse xenograft model to determine if MT19C would decrease tumor burden in vivo.

Methods: Safety studies were performed initially. Twenty nude mice were injected intraperitoneally every other day with either 0.3cc of vehicle (PBS + Ethanol) or 5mg/kg MT19C. Biweekly weights were
taken, as well as serum calcium levels on days 4 and 90. Mice were euthanized on day 90 or per animal protocol guidelines.

Thirty additional nude mice were injected subcutaneously with $5 \times 10^6$ SKOV-3 (75% matrigel / 25% PBS) cells in the flank. Once tumors reached a diameter of 6mm or greater, the mice were treated intraperitoneally every other day with either 0.3 cc of 5 mg/kg MT19c or vehicle. Mice were weighed biweekly and euthanized for tumor diameter greater than 20 mm, tumor ulceration or per animal protocol. Tumor diameter and was measured twice a week. A total of 30 treatments were given and then the remaining mice were euthanized.

**Results:** Serum calcium levels on day 40 were no different between the treatment group (8.96, SD 0.35) and control (10.00, SD 1.86). On day 90 of treatment the calcium levels increased equally in both groups, control 11.13 (SD 0.33) versus treatment 10.02 (SD 1.21).

Tumor diameters did not significantly differ on day 0 of treatment, control 6.6mm (SD 2.4) versus treatment 7.8mm (SD 2.8). On treatment day 20, control 13.5 mm (SD 2.5) versus treatment 9.9 mm (SD 4.3). By treatment day 40 there was a significant reduction in tumor diameter among the treatment group, control 16.9 mm (SD 3.2) versus treatment 7.1 mm (SD 5.44). At the end of the 30 treatments, 6 of 8 remaining mice in the treatment group had complete resolution of their tumors. The tumor diameter was significantly lower among the treatment group 2.1 mm (SD 4.0) versus control 18.4 mm (SD 1.5).

**Conclusion:** MT19C significantly decreased tumor burden in an ovarian cancer xenograft mouse model without significant toxicity. Complete resolution of tumors occurred in the majority of mice completing treatment. This drug appears to be a potentially potent chemotherapeutic agent.