Late-Breaking Abstracts
2015 Society of Gynecologic Oncology
Annual Meeting on Women's Cancer®

Opening Scientific Session
Saturday, March 28, 2015
Moderators: Uziel Beller, MD, *Shaare Zedek Medical Center, Jerusalem, Israel*
Joel I. Sorosky, MD, *Abington Memorial Hospital, Abington, PA, USA*
Farr R. Nezhat, MD, FACOG, FACS, *St. Luke's-Roosevelt Hospital, New York, NY, USA*

3 - Scientific Plenary (Late-Breaking Abstract)
A phase III randomized controlled clinical trial of carboplatin and paclitaxel alone or in combination with bevacizumab followed by bevacizumab and secondary cytoreductive surgery in platinum-sensitive, recurrent ovarian, peritoneal primary and fallopian tube cancer (Gynecologic Oncology Group 0213)
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Objectives: Platinum-based doublets have become a standard of care for women with platinum-sensitive recurrent ovarian cancer. The roles of secondary surgery and addition of bevacizumab have yet to be defined as neither intervention has demonstrated an improvement in overall survival in a phase III trial. GOG0213 sought to examine both.
Methods: GOG0213 is a bifactorial, randomized, phase III trial with two primary objectives: (1) to examine the role of bevacizumab(15 mg/kg) in combination with paclitaxel (175mg/m²) + carboplatin(AUC5) followed by bevacizumab maintenance and (2) to examine the role of secondary cytoreduction before initiation of chemotherapy. The primary endpoint for both objectives is overall survival (OS). Secondary endpoints include: safety/toxicity, allergy (HSR), progression-free survival (PFS), and intervention-dependent quality of life (QoL). Three strata were prospectively defined: participation on Objective 2, Platinum-free interval (6-12, >12 months) and prior bevacizumab treatment. Chemotherapy randomization for Objective 1 terminated on 8/29/11 and matured for OS (n=214 events in the control arm) on 11/5/2014. Enrollment for Objective 2 is ongoing.
Results: Six-hundred-seventy-four patients (n=567, Objective 1; n=107, Objectives 1 and 2) were randomized to CT (n=374) or CTB (n=374) and evaluable for OS. Equal representation in each treatment arm was observed for each stratum (Objective 2 (y/n): 53/54; PFI: 6-12/12+:181/493; Prior bevacizumab (y/n): 67/606). Median age: 60 and predominant histology was serous: 81%. Relative to CT, CTB improved the stratified estimated treatment hazard ratio (HR) of death by 18.6% [HR_{OS}: 0.827 (95%CI:0.683-1.005), p=0.056) corresponding to a median OS of 42.2 vs 37.3 mos. PFS was similarly improved by CTB (HR_{PFS}: 0.614, 95%CI:0.522-0.722, p<0.0001), corresponding to a median PFS of 13.8 mos vs. 10.4 mos). CTB was associated with more toxicity relative to CT (Table). HSR (all grades, CT vs CTB) occurred in 25.1% and 26.7% (p=0.66), respectively. QoL measures are being analyzed.
Conclusions: GOG0213 increased OS when women with platinum-sensitive recurrent ovarian cancer were treated with CTB. The adjusted HR borders statistical significance. CTB was associated with more toxicity but no unexpected safety signals were observed.

Toxicity (grade 3+)	CT	CTB	P
GI perforations necrosis fistula (any grade)	4%	14.8%	<0.001
GI perforations necrosis fistula	1%	1.8%	0.5
Infections	5.8%	13.0%	0.002
Joint pain	4.6%	15.1%	<0.001
Proteinuria	0%	8.1%	<0.001
Venous thrombosis	1.2%	3.9%	0.046
Arterial thrombosis	0.6%	2.4%	0.107
Febrile neutropenia	2.7%	6.1%	p=0.056

Scientific Plenary VII: Late-Breaking Abstract Session
Monday, March 30, 2015
Moderator: David Cohn, MD, *The Ohio State University, Columbus, OH, USA*
Martee Hensley, MD, *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

1 – Late-Breaking Abstract
Phase III SCORPION trial (ID number: NCT01461850) in epithelial ovarian cancer patients with high tumor load receiving PDS versus NACT: An interim analysis on peri-operative outcome
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Objectives: The SCORPION trial compared perioperative and survival outcome of primary debulking surgery (PDS) versus neo-adjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) in high tumor load advanced epithelial ovarian cancer patients (AEOC). The aim of this study was to perform an ad interim analysis with respect to the safety (i.e. peri-operative morbidity and mortality) of the trial.

Methods: Patients' eligibility criteria were: pathologically proven ovarian cancer, 18 to 75 years old, ECOG performance status ≤ 2, FIGO stage IIIC-IV, no history of other cancers, intra-operative high tumor load assessed by staging laparoscopy (i.e. Fagotti's score between 8 and 12). Exclusion criteria were: intra-operative mesenteral retraction and miliary carcinosis on the bowel. Women were randomly assigned to PDS or NACT–IDS arm. Surgical data were evaluated by univariate analysis. Intra- and post-operative complications were assessed using the MSKCC surgical secondary events grading system. Survival data were not shown because the events were too far to reach the medians in both arms at this time.

Results: Between October 2011 and November 2014, 200 suspicious AEOC women were eligible for the study, but only 110 were intra-operatively randomized. There were no significant differences between the two groups in the pre-operative characteristics and intra-operative tumor dissemination. Upper abdominal procedures were performed in 100% and 61.1% of the patients in the PDS and NACT-IDS arms, respectively (P = 0.0001). The percentages of optimal residual tumor (RT ≤ 1 cm) at PDS and IDS were 91% and 90% respectively, with a rate of complete cytoreduction (RT=0) of 45.0% and 60.0%, respectively (P = 0.158). Major postoperative complication rates (MSKCC score ≥ 3) of the PDS and NACT-IDS groups were 52.6% (29/55) and 6.0% (3/55), respectively (P = 0.0001). Postoperative mortality rate was 3.6% (2/55) and 0% (0/55) in the PDS and NACT-IDS groups, respectively (P = 0.154).

Conclusions: PDS is associated with a statistically significant higher risk of severe peri-operative morbidity with respect to NACT-IDS in high tumor load AEOC patients. Hence, waiting for survival data, we should be very careful in choosing the primary approach in this specific setting of women outside of a clinical trial.

Table. Operative and post-operative details

Variable	PDS Nr. (%)	NACT-IDS Nr. (%)	*p value*
All cases	55	55	n.a.
Upper Abdominal Procedures (UAP) Yes No	0 55 (100)	33 (61.1) 21 (38.9)	**0.0001**
Surgical complexity score groups * 1 2-3	0 55 (100)	29 (53.7) 25 (46.3)	**0.0001**
Size of residual disease No gross 0.1-1 cm > 1 cm	25 (45.5) 25 (45.5) 5 (9.0)	30 (60.0) 15 (30.0) 5 (10.0)	0.158
Major post-operative complications ** 3 4 5	24 (43.6) 3 (5.4) 2 (3.6)	3 (6.0) 0 0	**0.001**
Median operative time (min) (range)	451 (230 - 720)	275 (70 – 400)	**0.0001**
Median blood loss (ΔHb g/dl) (range)	3.25 (0.02 - 5.10)	1.40 (0.01 - 6.20)	**0.001**
Patients transfused	15 (27.3)	5 (9.3)	**0.015**
Median hospital stay (dys) (range)	12 (3-80)	6 (2-13)	**0.0001**
Median days to start to start CT (range)	40 (17 - 120)	20 (6 - 40)	**0.0001**

*According to Aletti et al. (1)

**According to Memorial Sloan-Kettering Cancer Center surgical secondary events grading system (2)

1. Aletti GD, Eisenhauer EL, Santillan A, Axtell A, Aletti G, Holschneider C, Chi DS, et al. Identification of patient groups at highest risk from traditional approach to ovarian cancer treatment. Gynecol Oncol. 2011 Jan;120(1):23-8
2. Chi DS, Franklin CC, Levine DA, Akselrod F, Sabbatini P, Jarnagin WR, DeMatteo R, et al. Improved optimal cytoreduction rates for stages IIIC and IV epithelial ovarian, fallopian tube, and primary peritoneal cancer: a change in surgical approach. Gynecol Oncol 2004;94:650–4.

2 – Late-Breaking Abstract

A phase II evaluation of cediranib in the treatment of recurrent or persistent endometrial cancer: An NRG Oncology/Gynecologic Oncology Group (GOG) study

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Objectives: Cediranib is a multi-tyrosine kinase inhibitor targeting vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and fibroblast growth factor (FGF) receptors. This phase II study was conducted to assess the activity and tolerability of single-agent cediranib in recurrent or persistent endometrial cancer.

Methods: Eligible patients had recurrent or persistent endometrial cancer after receiving one or two prior cytotoxic regimens, measurable disease, and a Gynecologic Oncology Group performance status of <2 (<1 if two prior cytotoxic regimens given). Cediranib 30 mg orally daily for a 28-day cycle was administered until disease progression or prohibitive toxicity. Microvessel density (MVD) was measured in the initial hysterectomy specimens and correlated with clinical outcome. Primary endpoints were tumor response and surviving progression-free for six months without subsequent therapy (6-month event free survival [EFS]).

Results: Of 53 patients enrolled, 48 were evaluable for cediranib efficacy and toxicity. Median age was 65.5 years. Fifty two percent of patients had received prior radiation, and 73% of patients received only one prior chemotherapy regimen. A partial response was observed in 12.5%. Fourteen patients (29%) had six-month EFS. Median progression-free survival (PFS) was 3.65 months and median overall survival (OS) was 12.5 months. No grade 4 or 5 toxicities were observed. A trend towards improved PFS was found in patients whose tumors expressed high MVD.

Conclusions: Cediranib as a monotherapy treatment for recurrent or persistent endometrial cancer is well tolerated and has met protocol set objectives for sufficient activity to warrant further investigation. MVD may be a useful biomarker for activity.

3 – Late-Breaking Abstract

Association between quality of life and clinical outcome in women with advanced epithelial ovarian cancer receiving chemotherapy with concurrent and maintenance bevacizumab: Results from a prospective multicenter phase III NRG Oncology/Gynecologic Oncology Group (GOG) trial

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Objectives: Evaluate the ability of a validated health-related quality of life (HRQOL) assessment tool, the FACT-O TOI questionnaire, to independently predict progression-free (PFS) and overall survival (OS) in women with advanced epithelial ovarian cancer (EOC) receiving chemotherapy with and without concurrent and maintenance bevacizumab.

Methods: Patients enrolled in GOG 218 who completed FACT-O TOI assessments prior to randomization (baseline) and had at least one follow-up assessment during study therapy were eligible. Baseline FACT-O TOI scores were sorted by quartiles (Q1-4), and outcomes were compared between Q1 (lowest) and Q2-4 with log-rank statistics. Trends in FACT-O TOI scores from baseline to the latest recorded follow-up assessment were evaluated for impact on intragroup (Q1 or Q2-4) outcome by log-rank analysis. A multivariate Cox proportional hazards model considered PFS and OS adjusting for stage IV disease, performance status (PS), and assigned treatment group (+/- bevacizumab with adjuvant and maintenance therapy).

Results: Of 1,152 eligible patients, 283 had FACT-O TOI scores in Q1 and 869 had scores in Q2-4 groups. Mean baseline FACT-O TOI scores were 47.5 for Q1 vs. 74.7 for Q2-4 ($P < 0.0001$). Patients with Q1 scores were significantly more likely to have stage 4 disease (30% vs. 24%, $P = 0.04$) and PS of 2 (15% vs. 3%, $P < 0.0001$). Q1 FACT-O TOI baseline scores were associated with worse OS compared to Q2-4 scores (37.5 vs. 45.6 months, $P = 0.005$). Improved compared to worsened serial FACT-O TOI scores relative to baseline were significantly associated with longer PFS (Q1: 12.7 vs. 8.6 months, $P = 0.001$; Q2-4: 16.7 vs. 11.1 months, $P < 0.0001$) and OS (Q1: 40.8 vs. 16 months, $P < 0.0001$; Q2-4: 54.4 vs. 33.6 months, $P < 0.0001$). In multivariate analysis Q2-4 patients at baseline had a significantly decreased risk of disease progression (hazard ratio [HR] 0.994, 95% confidence interval [CI] 0.990-0.999, $P = 0.013$), and death (HR 0.992, 95%CI 0.987-0.997, $P = 0.002$).

Conclusions: Baseline FACT-O TOI scores were independently predictive of PFS and OS while serial FACT-O TOI scores showing improved vs. worsened quality of life were associated with significantly better PFS and OS in women with advanced ovarian cancer. Further evaluation is warranted to determine the predictive utility of this HRQOL tool.

4 – Late-Breaking Abstract

Impact of NCI Comprehensive Cancer Centers on ovarian cancer treatment and survival

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Objectives: To determine the regional impact of care at a National Cancer Institute Comprehensive Cancer Center (NCI-CCC) on adherence to National Comprehensive Cancer Network (NCCN) ovarian cancer treatment guidelines and survival.

Methods: Retrospective population-based study of consecutive patients diagnosed with epithelial ovarian cancer between 1/1/96 and 12/31/06 in southern California were stratified according to care at an NCI-CCC (n=5), non-NCI high-volume hospital (≥10 cases/year, HVH, n=29), or low-volume hospital (<10 cases/year, LVH, n=158). Multivariable logistic regression and Cox-proportional hazards models were used to examine the effect of NCI-CCC status on treatment guideline adherence and ovarian cancer-specific survival.

Results: A total of 9,933 patients were identified (Stage I=22.8%, Stage II=7.9%, Stage III=45.1%, Stage IV=24.2%), and 8.1% of patients were treated at NCI-CCCs. Overall, 35.7% of patients received NCCN guideline adherent care. NCI-CCC status (OR=1.00) was an independent predictor of adherence to treatment guidelines compared to HVHs (OR=0.83, 95%CI=0.70-0.99) and LVHs (OR=0.56, 95%CI=0.47-0.67). The median ovarian cancer-specific survival according to hospital type was: NCI-CCC=77.9 (95%CI=61.4-92.9) months, HVH=51.9 (95%CI=49.2-55.7) months, and LVH=43.4 (95%CI=39.9-47.2) months ($P < 0.0001$). The survival advantage associated with NCI-CCC status was maintained across socioeconomic strata. NCI-CCC status (HR=1.00) was a statistically significant and independent predictor of improved survival compared to HVH (HR=1.18, 95%CI=1.04-1.33) and LVH (HR=1.30, 95%CI=1.15-1.47).

Conclusions: NCI-CCC status is an independent predictor of adherence to ovarian cancer treatment guidelines and improved ovarian cancer-specific survival. These data validate NCI-CCC status as a structural health care characteristic correlated with superior ovarian cancer quality measure performance. Increased access to NCI-CCCs through regional concentration of care may be a mechanism to improve clinical outcomes.

5 – Late-Breaking Abstract

A phase II evaluation of sunitinib (SU11248) in the treatment of persistent or recurrent clear cell ovarian carcinoma: An NRG Oncology/Gynecologic Oncology Group (GOG) study

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Objectives: Sunitinib (SU11248) is an oral multi-targeted tyrosine kinase inhibitor against vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) pathways which are involved in tumor progression of clear cell cancers. We studied its efficacy and tolerability in persistent or recurrent clear cell ovarian cancer patients.

Methods: All patients received one or two prior regimens, measurable disease, and GOG performance status of at least 2. Tumors must be at least 50% clear cell histomorphology and negative for expression of WT-1 antigen and Estrogen Receptor antigen by immunohistochemistry. Sunitinib 50 mg per day for 4 weeks was administered in repeated 6-week cycles until disease progression or prohibitive toxicity. Primary end points were progression-free survival (PFS) at 6 months and clinical response. The study was designed to determine if the drug had a response rate of at least 20% or PFS at 6 months of 25%.

Results: From 2010-2014, 35 patients were enrolled and 30 were treated and eligible (median age: 51, range: 27 to 73). Twenty-five (83%) were Whites, 4 (13%) Asians, and 1 (3%) unknown. Performance statuses of 0, 1, and 2 comprised of 18, 10, and 2 patients. Five (16.7%) patients had PFS ≥ 6 months (90%CI: 6.8%, 31.9%). Two (6.7%) patients had a partial or complete response (90%CI: 1.2%–19.5%). The median PFS was 2.7 months. The median overall survival was 12.8 months. The most common grade 3 adverse events were fatigue (4), hypertension (4), neutropenia (4), anemia (3), abdominal pain (3), and leukopenia (3). Grade 4-5 adverse events included thrombocytopenia (5), anemia (2), acute kidney injury (1), stroke (1), and allergic reaction (1).

Conclusions: Sunitinib demonstrated minimal activity in the second- and third-line treatment of persistent or recurrent clear cell ovarian carcinoma.

6 – Late-Breaking Abstract

Sentinel lymph node mapping accurately identifies positive nodes in women with high risk endometrial cancer

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Objectives: The role of sentinel lymph nodes (SLN) and preoperative PET/CT continues to evolve in the surgical staging of endometrial cancer (EC). The purpose of this study was to identify the sensitivity, specificity and false negative rate of SLN when compared to complete pelvic and para-aortic lymphadenectomy (LAD) in high risk EC and to determine the utility of preoperative PET/CT.

Methods: Women with high risk EC (grade 3, serous, clear cell) were prospectively enrolled. They underwent preoperative PET/CT, intraoperative lymphatic mapping, SLN removal followed by complete pelvic and para-aortic (LAD) up to the renal vessels. Patients were evaluable if SLN mapping was attempted and a full LAD was performed. Sensitivity, specificity, and 95%CI were calculated for SLN.

Results: Of the planned 100 patients, to date 73 were enrolled between April 2013 and February 2015; 60 were evaluable. Median age was 61.1 years (range 29.2 - 87.0). Median BMI was 30.1 kg/m² (range 15.8 - 64.3). Lymphatic mapping was performed using indocyanine green (n = 34; 61.8%), blue dye only (n = 13; 23.2%), or blue dye + technetium (n = 9; 16.4%). At least one SLN was identified in 56/60 (92.3%) patients; 37 (60.7%) had bilateral pelvic SLN, 17 (28.3%) unilateral pelvic SLN, and 2 (3.3%) para-aortic SLN. Eleven of fifty-six patients (19.6%) had > 1 SLN positive for metastatic disease. Among these, 4/11 (36.4%) also had non-sentinel nodes positive for disease. The median size of the metastatic deposit in the node for patients who had +SLN only was 3.8 mm (range 1.7 - 5.1). For each patient with a node positive for metastatic disease, at least one SLN was also positive for metastatic disease for a sensitivity of 100% (95%CI 77.0%, 100.0%) and specificity of 100% (95%CI, 94.4%, 100%). While there were no false negative cases, one patient had a left sided SLN biopsy positive for metastatic disease and right-sided false negative SLN. Among the 9 patients who had positive nodes on preoperative PET/CT, only 2 had histologically positive nodes.

Conclusions: In our preliminary results, SLN mapping was able to identify all women with IIIC high risk endometrial cancer with a false-negative rate of 0%. Sentinel lymph node biopsy alone could be considered in women with high risk EC.

7 – Late-Breaking Abstract

Preoperative risk assessment for lymph node metastasis in endometrial cancer (PALME study): Results of the Korean Gynecologic Oncology Group study

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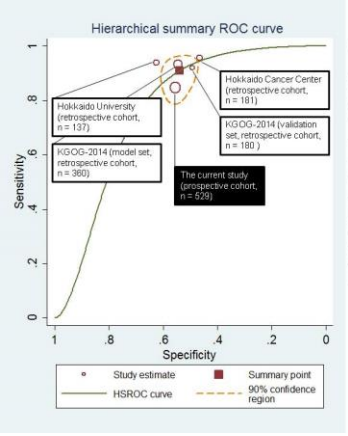
Objectives: To confirm the reliability of the previously suggested preoperative risk criteria for lymph node metastasis in endometrial cancer (Kang et al. *J Clin Oncol*. 2012), the Korean Gynecologic Oncology Group conducted an international, multi-center, prospective validation study. (PALME study, ClinicalTrials.gov identifier NCT01527396)

Methods: Between 2012 and 2014, 529 patients (median age, 59 years) with histologically diagnosed endometrial cancer who underwent surgical staging including systemic pelvic and/or para-aortic lymphadenectomy were prospectively enrolled from 25 centers across three countries (Korea, Japan and China). The following criteria were used for identifying a low-risk group for nodal metastasis: 1) endometrioid-type histology in preoperative biopsy, 2) MRI findings corresponding with FIGO stage IA, 3) serum CA125 levels ≤ 35 U/mL, and 4) no evidence of gross metastasis at surgery. The primary endpoint was a negative predictive value higher than 96%.

Results: Nodal metastasis was found in 52 of 529 patients (9.8%). The median number of harvested lymph nodes was 23. Among the 272 patients (51.4%) identified as a low-risk group, lymph node metastasis was found in 8 patients (2.9%, negative predictive value = 97.1%). The sensitivity and specificity of the criteria were 84.9% and 55.5%, respectively. When CA125 was replaced by preoperative tumor grade, the specificity significantly decreased to 50.2% (P = 0.0073), whereas the sensitivity did not change (88.7%, P = 0.5). False negative prediction was associated with unfavorable histology (non-endometrioid histology or grade 3 disease) in post-operative biopsy (P = 0.046).

Conclusions: The MRI-based preoperative risk criteria reliably identify a low-risk group for nodal metastasis in endometrial cancer. Using serum CA125 levels instead of tumor grade significantly improves the specificity of the prediction model.



Figure

Performance of the KGOG preoperative criteria for a low-risk group for lymph node metastasis in the current and previous studies

A hierarchical summary receiver operating characteristic curve (HSROC) for the diagnostic performance of the KGOG criteria (green line). Each circle represents a study and the size of the circle is proportional to the sample size of each study. The summary point (filled box) represents the summarized specificity and sensitivity (91% and 54%, respectively). 90% confidence intervals for those operating points are shown (dotted line).

8 – Late-Breaking Abstract

Tumor *BRCA* mutation or high genomic LOH identify ovarian cancer patients likely to respond to rucaparib: Interim results for ARIEL2 clinical trial

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Objectives: At least 50% of high-grade serous ovarian cancers (OC) may have homologous recombination deficiency (HRD). Germline *BRCA1* and *BRCA2* mutations (*gBRCA^{mut}*) account for ~1/3. Prospective identification of non-*gBRCA^{mut}* HRD OC tumors likely to respond to a PARP inhibitor remains challenging. A next-generation sequencing (NGS) assay and analysis algorithm were developed to predict rucaparib sensitivity by detecting tumor *BRCA* status and high genomic loss of heterozygosity (LOH). This HRD assay and algorithm are being prospectively validated in Phase 2 study ARIEL2 (NCT01891344).

Methods: ARIEL2 evaluates rucaparib in 180 pts with platinum-sensitive, measurable, high-grade serous or G2/3 endometrioid OC. The primary objective is to evaluate clinical activity of 600 mg bid rucaparib in 3 HRD subgroups: tumor *BRCA*^{mut}, *BRCA*^{wt}/LOH^{high} and *BRCA*^{wt}/LOH^{low}. Enrollment of known *gBRCA*^{mut} pts

is limited to focus on other response predictors. Tumor HRD status is assessed using a pre-treatment biopsy or archival tissue. Response is assessed by RECIST v1.1 and GCIG CA125 criteria.

Results: Data are presented for the first 61 pts (median age=64 [range 44-86], 69% ECOG=0, 97% high-grade serous; 54% with ≥2 prior regimens) with available NGS assay and efficacy results. Treatment-related AEs in ≥15% of pts were GI symptoms (nausea, dysgeusia, decreased appetite, constipation, vomiting, diarrhea), fatigue, ↓ Hgb, ANC, and platelets, ↑ creatinine, and transient ↑ ALT/AST without other evidence of liver dysfunction. Efficacy data indicate the HRD assay and algorithm identify tumors sensitive to rucaparib. The objective response rates (RECIST+CA125) are 70%, 48% and 8% in *BRCA*^{mut}, *BRCA*^{wt}/LOH^{high} and *BRCA*^{wt}/LOH^{low} pts, respectively (Table 1, $P < 0.001$, Cochran-Armitage trend test).

Conclusions: Rucaparib exhibited robust activity in HRD tumors and was well tolerated. Efficacy data for 61 pts indicate a tumor HRD assay and algorithm combining *BRCA* mutation and genomic LOH analysis identifies OC pts likely to respond to rucaparib. The HRD signature will be applied prospectively to analysis of ARIEL3 (NCT01968213), a Phase 3 maintenance study in a similar population.

Table 1. Response by HRD Status

HRD Subgroup	# of Pts	RECIST ORR, %	RECIST & GCIG CA-125 ORR, %
BRCA^{mut}	23	65	70
BRCA^{wt}/LOH^{high}	25	36	48
BRCA^{wt}/LOH^{low}	13	8	8