

Abstracts Presented for the 47th Annual Meeting of the Society of Gynecologic Oncology

Scientific Plenary VIII: Late-breaking Abstract Session

Monday, March 21, 2016

Moderators: Rebecca L. Stone, MD, *University of Arkansas for Medical Sciences, Little Rock, AR, USA*

Krishnansu S. Tewari, MD, *UC Irvine Medical Center, Orange, CA, USA*

1 – Late-breaking Abstract Session

Response after 3 cycles of first-line platinum chemotherapy in advanced ovarian cancer: An analysis of the neoadjuvant arm of CHORUS

S. Kehoe. *University of Birmingham, Birmingham, United Kingdom of Great Britain and Northern Ireland*

Objectives: To ascertain the responses achieved after 3 cycles of platinum-based chemotherapy in women randomized to the neoadjuvant arm of the CHORUS trial.

Methods: CHORUS, a noninferiority trial, compared the outcome of primary surgery followed by neoadjuvant chemotherapy and delayed surgery after 3 cycles of therapy. A total of 552 women were recruited between March 2004 and August 2010. Of these, 550 were suitable for analysis. Women mainly had advanced and bulky tumors, were older (median age, 65 years), and 19% had a WHO performance status of 2/3. Progression-free and overall survival showed the neoadjuvant arm was noninferior to the control arm. The trial database was scrutinized to obtain information regarding response rates.

Results: Of 274 women randomized to the neoadjuvant arm, 253 began chemotherapy, of whom 217 underwent surgery. Of 36 women who did not have surgery, 17 had progressive disease or died; no disease was present in 5; 2 were ineligible; 1 patient refused; and 11 others were deemed unsuitable for surgery. Preoperative computed tomography assessment of disease was categorized as 'no disease,' 'stable,' or 'progressive' found that 10 (4%) women had no disease (all had surgery); 204 (87%) had stable disease, of whom 14 did not undergo surgery; and 21 (9%) had progressive disease (13 of whom did not have surgery). Data were unavailable on 18 patients (9 of whom did not have surgery). At laparotomy (n = 217), the diameter of disease observed before resection showed that 7 (4%) women had no macroscopic disease, 24 (12%) had 1 cm or less, and 166 (84%) more than 1 cm. The corresponding statistics in the control arm patients, who underwent surgery were 2%, 6% and 92%, respectively. Data were unavailable for 20 other women. Serum CA-125 concentration decreased 50% in 67% of women at their immediate preoperative cycle, and at least 50% in the 2 cycles before surgery in 34% of women. Thus according to GCIG criteria, at least 34% of women had a CA-125 response. CA-125 levels normalized in 10% of women. No correlation was noted between CA-125 decrease and the disease evaluation at laparotomy

Conclusions: After 3 cycles of platinum-based chemotherapy, preoperative treatment achieved complete response in 4% based on imaging/surgical finding and 10% based on serum CA-125 levels. The overall CA-125 response rate is estimated to be at least 34%.

2– Late-breaking Abstract Session

A prospective randomized trial comparing colorimetric and fluorescent imaging for pelvic sentinel lymph node mapping in endometrial cancer

R.W. Holloway, S. Ahmad, J.E. Kendrick IV, G.E. Bigsby IV, L.A. Brudie, G.B. Ghurani, N.M. Stavitzski, J.L. Gise, S.B. Ingersoll and J.W. Pepe. *Florida Hospital Cancer Institute, Orlando, FL, USA*

Objectives: To prospectively compare sentinel lymph node (SLN) mapping using isosulfan blue (ISB) with indocyanine green (ICG) using near-infrared imaging in patients with apparent uterine-confined endometrial cancer (EC). Our aims were to: (1) test the null hypothesis of no difference between ISB detection of SLN versus ISB + ICG in a randomized clinical trial, and (2) determine sensitivity and negative predictive value for detection of lymph node (LN) metastasis.

Methods: Following US Food and Drug Administration and institutional review board approvals, 200 endometrial cancer patients were enrolled (September 2012 to January 2015) with 5 surgeons. Patients were randomized using SAS version 9.2, with 10% cases allocated to ISB alone. ISB (2 mL) and ICG (2 mL; 1 mg/mL) were injected into the cervix, 2 to 5 mm below the mucosa. All patients underwent robotic-assisted hysterectomy with pelvic ± aortic lymphadenectomy. Retroperitoneal spaces were opened and ISB results recorded on all 200 cases. Envelopes were opened and near-infrared imaging was used per randomization cards on 180 subjects.

Results: A total of 180 cases were mapped with ISB + ICG (group A), and 20 cases were randomized to ISB alone (group B). Mean age was 64.5 ± 8.4 years and body mass index was 33 ± 8 kg/m². Histologies included endometrioid G1 (43%), G2 (30%), G3 (7%), and type II (20%). Pathology characteristics included lymphovascular space invasion (31.5%), DOI more than 50% (27.5%), lesion size greater than 2 cm (77%). Mean time from dye injection to opening of spaces was 10.3 ± 6 minutes and time to complete mapping with LN removal was 22.4 ± 9.4 minutes. Operating room time was 136 ± 36 minutes, total LN were 23.1 ± 10.7 . Group A ISB detection of SLN was not different from that of control group B ($P = .35$). SLN detection for ISB + ICG group A ($n = 180$) versus all ISB ($n = 200$) were as follows: bilateral—83.9% versus 40%; unilateral—12.2% versus 36%; and none—3.9% versus 24%, $P < .001$). Median SLN per case in group A was 2 (range, 0–4). Positive SLNs were found in 39 group A (21.7%) and 2 group B cases (10%). There was 1 false-negative SLN (97.5% sensitivity, 99.3% negative predictive value, 2.5% false-negative rate). SLN was the only positive LN in 25 (62.5%) of 40 node-positive cases. Isolated tumor cells were found in 11 (28.2%) of 39 SLNs compared with 2 (14.3%) of 14 non-SLN metastases. ISB improved the ICG detection of SLNs (3 bilateral, 10 unilateral, 1 LN metastasis). No allergic reactions to either dye were seen.

Conclusions: ISB + ICG and near-infrared imaging detected more SLN and LN metastases than ISB alone in this phase III trial. SLN mapping with ICG + ISB had excellent sensitivity for detection of metastasis.

3 – Late-breaking Abstract Session

Preliminary results of a phase II study: PD-1 blockade in mismatch repair-deficient, recurrent or persistent endometrial cancer

A.N. Fader^a, L.A. Diaz^b, D.K. Armstrong^c, E.J. Tanner III^d, J. Uram^a, A. Eyring^a, H. Wang^a, G. Fisher^e, T. Greten^f and D. Lea^a. ^aJohns Hopkins School of Medicine, Baltimore, MD, USA, ^bJohns Hopkins University, Baltimore, MD, USA, ^cJohns Hopkins Kimmel Cancer Center, Baltimore, MD, USA, ^dJohns Hopkins Hospital, Baltimore, MD, USA, ^eStanford University School of Medicine, Stanford, CA, USA, ^fNational Cancer Institute, Bethesda, MD, USA

Objectives: Mismatch repair (MMR) deficiency is present in 20% to 30% of endometrial cancers (EC). MMR-deficient tumors harbor thousands of mutant neoantigens and may be sensitive to immune augmentation therapy with programmed death-1 (PD-1) blockade. The study objective was to assess the preliminary response rates and survival outcomes in women with MMR-deficient recurrent or persistent EC after treatment with pembrolizumab (a potent, highly selective humanized monoclonal antibody of the IgG4/kappa isotype, which blocks the interaction between PD-1 and its ligands).

Methods: This is an ongoing, single-institution phase II study evaluating the clinical efficacy of anti-PD-1, pembrolizumab, in patients with previously treated, measurable, recurrent, or persistent cancer with MMR deficiency. This includes a subset of patients with EC. Patients must have received at least 1 line of prior standard-of-care therapy, and may have received up to 4 previous regimens. Pembrolizumab was delivered intravenously at a dose of 10 mg/kg every 2 weeks. The primary endpoint was response rate, and patients were assessed for response every 8 weeks with a computed tomography scan.

Results: As of January 10, 2016, 9 patients with EC who failed prior therapy (median, 2 prior therapies) have enrolled and completed at least 1 evaluation. All study subjects have endometrioid histologies. The median follow-up duration is 9.1 months (range, 7–18 months). Thus far, there have been no toxicities higher than grade 3. To date, the overall response rate is 56% (95% CI 21%–86%, $n = 5$), with 1 complete response (CR) and 4 partial responses (PR). The disease control rate, or “clinical benefit” rate (CR + PR + stable disease), is 88.9% ($n = 8$). The 12-month overall survival (OS) rate is 89%, and the median OS has not been reached. Of the 2 patients with

progression, 1 had only an increase of small-volume disease in the liver and retroperitoneum, with a PR observed in multiple pulmonary nodules (i.e., mixed response). She remains on the study drug 6 months after disease progression and is asymptomatic. Before enrolling on this trial, the patient with a CR had previously undergone 3 surgeries and received 3 previous lines of treatment. She has been without evidence of disease for 17 months.

Conclusions: PD-1 blockade shows promising activity in MMR-deficient EC. A cooperative group study of PD-1 blockade in a larger cohort of women with both MMR-deficient and MMR-intact, recurrent or persistent EC is planned.

4 - Late-breaking Abstract Session

NRG/GOG 186K: A randomized phase II study of NCI-supplied cabozantinib versus weekly paclitaxel in the treatment of persistent or recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer—Final results

U.A. Matulonis^a, M. Sill^b, P.H. Thaker^c, J.W. Carlson^d, C.J. Darus^e, R.S. Mannel^f, D.P. Benders^g, R.V. Higgins^h and C. Aghajanianⁱ. ^aDana-Farber Cancer Institute, Boston, MA, USA, ^bGynecologic Oncology Group Statistical and Data Center, Buffalo, NY, USA, ^cWashington University School of Medicine in St. Louis, St. Louis, MO, USA, ^dMercy Clinic - Women's Oncology, Springfield, MO, USA, ^eMaine Medical Partners, Scarborough, ME, USA, ^fUniversity of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, ^gUniversity of Iowa Hospitals and Clinics, Iowa City, IA, USA, ^hLevine Cancer Institute, Carolinas Medical Center, Charlotte, NC, USA, ⁱMemorial Sloan Kettering Cancer Center, New York, NY, USA

Objectives: Cabozantinib is an oral inhibitor of VEGFR2 and c-MET and has demonstrated activity in recurrent ovarian cancer in previous phase II trials. The primary objective of this study was to compare the progression-free survival (PFS) reached with cabozantinib with that of weekly paclitaxel in recurrent ovarian cancer.

Methods: PFS was assessed at 3.68 months (approximately before cycle 5/week 16) and 7.36 months (approximately before cycle 9/week 32) to see if cabozantinib delayed progression. Secondary objectives included response, toxicities, and survival. c-MET expression and copy number were examined for associations with outcome. Patients were randomized 1:1 (open-label) to either cabozantinib (60 mg orally daily continuously) or paclitaxel (80 mg/m² weekly on days 1, 8 and 15); one cycle equaled 28 days. Eligibility criteria included recurrent ovarian cancer, PS 0-2, and up to 3 prior treatment regimens. Patients were stratified based on platinum-free interval, measureable disease status, and prior bevacizumab therapy. The study had 85% power to detect a 43% reduction in the hazard when testing at the 10% level of significance with a Cochran-Mantel-Haenszel test.

Results: Between November 2012 and May 2014, 111 patients were enrolled. Primary analysis showed that the value of the Cochran-Mantel-Haenszel test was not significant ($P = .97$). Treatment with cabozantinib may be associated with an increased risk of progression ($P = .06$). The 2 regimens were comparable by toxicity except for gastrointestinal toxicities; cabozantinib had a higher rate of grade 3–4 gastrointestinal toxicities compared with paclitaxel (relative risk, 6.8; OR 9.0, 95% CI 1.88–84.3). Patients in the cabozantinib arm appeared to have stopped therapy sooner for disease progression or toxicity. Response for cabozantinib versus weekly paclitaxel was 8.3% versus 28.3, respectively. Median overall survival was 19.4 months for patients taking cabozantinib, and has not been reached yet for weekly paclitaxel (Cox HR 2.27, 90% CI 1.17–4.41).

Conclusions: The analysis of efficacy indicated that the dose and schedule of cabozantinib examined in this study was not interesting or worthy of further investigation.

5 – Late-breaking Abstract Session

Disease extent at secondary cytoreductive surgery is predictive of progression-free and overall survival: an NRG Oncology/Gynecologic Oncology Group study

P.G. Rose^a, J. Java^b, M.A. Morgan^c, A.A. Secord^d, J. Kesterson^e, F.B. Stehman^f, D.P. Warshal^g, W.T. Creasman^h, P. Hanjaniⁱ, R.T. Morris^j and L.J. Copeland^k. ^aCleveland Clinic, Cleveland, OH, USA, ^bGynecologic Oncology Group Statistical and Data Center, Buffalo, NY, USA, ^cUniversity of Pennsylvania Health System, Philadelphia, PA, USA, ^dDuke University Medical Center, Durham, NC, USA, ^ePenn State College of Medicine, Hershey, PA, USA, ^fIndiana University School of Medicine, Indianapolis, IN, USA, ^gCooper University Hospital, Camden, NJ, USA, ^hMedical University of South Carolina, Charleston, SC, USA, ⁱHanjani Institute for Gynecologic Oncology, Abington Memorial Hospital, Abington, PA, USA, ^jKarmanos Cancer Center/Wayne State University, Detroit, MI, USA, ^kThe Ohio State University, James Cancer Hospital, Columbus, OH, USA

Objectives: Gynecologic Oncology Group (GOG) 152 was a randomized trial of secondary cytoreductive surgery (SCS) in patients with suboptimal residual disease (residual tumor nodule >1 cm in greatest diameter) after primary cytoreductive surgery. The current analysis was undertaken to evaluate the impact of disease findings at SCS on progression-free (PFS) and overall survival (OS).

Methods: Among the 550 patients enrolled in GOG 152, 216 were randomly assigned after 3 cycles of cisplatin and paclitaxel to receive SCS. In 15 patients (7%), surgery was declined or contraindicated. In the remaining 201 patients, the operative and pathology reports were used to classify their disease status at the beginning of SCS as no gross disease/microscopically negative (n = 40; 18.5%), no gross disease/microscopically positive (n = 8; 3.7%), and gross disease (n = 153; 70.8%).

Results: The median PFS was 16.1 months for patients with no gross disease/microscopically negative, 13.5 months for those with no gross disease/microscopically positive, and 11.5 months for those with gross disease ($P = .006$). The median OS was 51.5 months for patients with no gross disease/microscopically negative, 42.6 months for those with no gross disease/microscopically positive, and 30.8 months for those with gross disease ($P = .008$).

Conclusions: Although, as previously reported, SCS did not change PFS or OS, operative and pathologic findings in those who underwent the procedure were predictive of PFS and OS. Surgical/pathological residual disease is a biomarker of response to chemotherapy and predictive of PFS and OS.

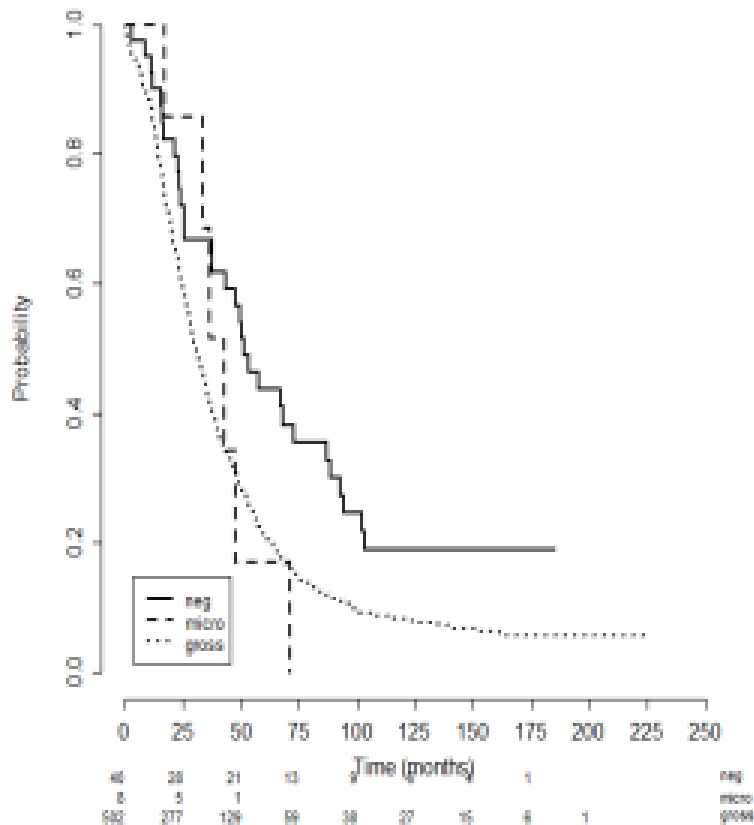


Fig. 1
Kaplan-Meier OS by Residual Disease.

6 – Late-breaking Abstract Session

A phase III trial of bevacizumab with IV versus IP chemotherapy for ovarian, fallopian tube, and peritoneal carcinoma: An NRG Oncology Study

J. Walker^a, M.F. Brady^b, P.A. DiSilvestro^c, K. Fujiwara^d, D. Alberts^e, W. Zheng^f, K. Tewari^g, D.E. Cohn^h, M. Powellⁱ, L. Van Lei^j, S. Rubin^k, S.A. Davidson^l, H.J. Gray^m, S. Waggonerⁿ, T. Myers^o, C. Aghajanian^m, A.A. Secord^p and R.S. Mannel^a. ^aThe University of Oklahoma, Oklahoma City OK, USA, ^bUniversity of Buffalo, Buffalo, NY, USA, ^cWomen & Infants Hospital, Providence, RI, USA, ^dSaitama Medical University International Medical Center, Hidaka-City, Saitama, Japan, ^eUniversity of Arizona Cancer Center, Tucson, AZ, USA, ^fUT Southwestern Medical Center, Dallas, TX, USA, ^gUniversity of California, Irvine Medical Center, Orange, CA, USA, ^hThe Ohio State University, Columbus, OH, USA, ⁱWashington University in St. Louis, St. Louis, MO, USA, ^jUniversity of North Carolina at Chapel Hill, Chapel Hill, NC, USA, ^kFox Chase Cancer Center, Philadelphia, PA, USA, ^lDenver Health Medical Center, Denver, CO, USA, ^mUniversity of Washington Medical Center, Seattle, WA, USA, ⁿUniversity Hospitals Case Medical Center, Cleveland, OH, USA, ^oBaystate Medical Center, Springfield, MA, ^pDuke University Medical Center, Durham, NC, USA

Objectives: To determine if one or both intraperitoneal chemotherapy (IP) regimens improve the progression-free survival (PFS) compared to intravenous (IV) chemotherapy for first-line treatment of patients diagnosed with optimally surgically resected stage II and III ovarian, peritoneal, or fallopian tube cancer.

Methods: Eligible patients had stage II-IV epithelial ovarian, peritoneal, or fallopian tube carcinoma. They were treated with bevacizumab 15mg/kg IV on cycles 2-22, and randomized to receive six cycles of: Arm 1) IV carboplatin AUC 6/ IV weekly paclitaxel 80 mg/m² (IV arm), or Arm 2) IP carboplatin AUC 6/ IV weekly paclitaxel 80 mg/m²/ (IP-carbo arm), or Arm 3) IV paclitaxel 135 mg/m² day 1/IP cisplatin 75 mg/m² day 2/IP paclitaxel 60 mg/m² day 8 (IP-cis arm).

Results: Among 1,560 trial participants, the median age was 58 years. Eighty-four percent had stage III disease, 72% had high grade serous histology, and 57% had no visible residual disease following optimal cytoreduction. Completion rates of platinum, taxane, or bevacizumab appear in Table 1. Cross-over to the IV-only therapy occurred in 16% randomized to IP carbo arm and 28% randomized to IP cis arm. Fifteen deaths possibly due to toxicity were relatively evenly distributed among treatment arms. Similarly, GI perforations/fistula/leak occurred in all three arms (range, 3.7% - 5.3%). While nearly 30% of patients in each arm reported grade 2+ peripheral neuropathy, treatment-induced HTN (20.5%) and grade 3/4 nausea and vomiting (11.2%) were observed more often in the IP cis arm. IP therapy did not confer a significant PFS advantage over IV only, with the median PFS by intent-to-treat being 24.9 (IV), 27.3 (IP carbo), and 26.0 mos (IP cis). Median PFS for stage II/III patients with 1 cm or less visible tumor was 26.8 (IV), 28.7 (IP carbo), and 27.8 mos (IP cis). Median PFS for stage III patients with no visible residual disease was 31.3, 31.8, and 33.8 months respectively. No statistically significant PFS benefit for IP was identified.

Conclusions: The progression free survival was not improved with IP chemotherapy. IV and IP carbo arms using weekly dose-dense paclitaxel were better tolerated than the IP cis arm. Neurotoxicity is a major problem on all arms. The reduced dose IP cisplatin regimen does not appear to be as effective as previously reported high dose cisplatin regimens. Survival data is not yet mature.

Table 1

Completion rates of platinum, taxane, or bevacizumab.

Treatment Arm	At least 6 cycles of Platinum	At least 6 cycles of Taxane	Median # bev cycles
IV only	90%	87%	20
IP carbo	91%	88%	18
IP cis	84%	87%	17

7 - Late-breaking Abstract Session

Patient-reported outcomes in GOG 252: NRG Oncology Study of IV vs IP chemotherapy for ovarian, fallopian, or peritoneal carcinoma

J.L. Walker^a, L. Wenzel^b, H. Huang^c and M.F. Brady^d. ^aThe University of Oklahoma, Oklahoma City, OK, USA, ^bUniversity of California, Irvine, Irvine, CA, USA, ^cGynecologic Oncology Group Statistical and Data Center, Buffalo, NY, USA, ^dUniversity of Buffalo, Buffalo, NY, USA

Objectives: To compare the patient-reported outcomes on (1) quality of life (FACT-O-TOI), (2) neuropathy (FACT-GOG/NTX4 scale), (3) abdominal discomfort (FACT-GOG/AD scale), (4) fatigue (FACIT-Fatigue scale), and (5) nausea (item from FACT-O-TOI).

Methods: Patient-reported outcomes will be assessed at 6 time points: (1) before randomization, (2) before the 4th cycle (9 weeks after starting treatment), (3) before the 7th cycle (18 weeks after starting treatment), (4) before the 13th cycle (36 weeks after starting treatment), (5) before the 21st cycle (60 weeks after starting treatment), and (6) 84 weeks after starting treatment. The instruments used were as follows: FACT-O-TOI, FACT-GOG/NTX4 scale, FACT-GOG/AD scale, FACIT-Fatigue scale, and FACT-O-TOI. Patient quality of life (QOL), neurotoxicity, and abdominal discomfort will be assessed with patient self-administered questionnaires. Assessments are timed to capture between-regimen active treatment differences (e.g., overall QOL, abdominal pain, nausea, fatigue) and between-regimen persistent long-term differences or emerging late effects (e.g., neuropathy).

Results: At week 84, there has been good compliance with form submission, and 80% of those expected have been submitted and are complete.

Conclusions: Analysis is under way and should be available in March 2016 to understand the patients' perspective on the tolerability of the 3 treatment arms. Reasons for discontinuation of assigned treatment will be assessed.