



IGCS 2022 Abstracts: Oral Abstract Presentations (Plenary Sessions)

Oral abstract presenters will present their abstracts in the below sessions.

The sessions will be live-streamed in real time onto the Meeting Portal and recorded for on-demand viewing from 24 hours after the session ends until December 28, 2022.

Plenary 01: Opening Ceremony and Oral Abstract Presentations

- Thursday, September 29, 2022
- 08:00 AM - 10:30 AM EDT
- Hall 501

Plenary 02: Oral Abstract Presentations

- Thursday, September 29, 2022
- 04:55 PM - 05:55 PM EDT
- Hall 501

Plenary 05: Oral Abstract Presentations & Closing Ceremony

- Saturday, October 1, 2022
- 03:55 PM - 05:25 PM EDT
- Hall 405

O001 / #504

Plenary Session

PLENARY 01: OPENING CEREMONY AND ORAL ABSTRACT PRESENTATIONS

29-09-2022 8:00 AM - 10:30 AM

DURVALUMAB, IN COMBINATION WITH AND FOLLOWING CHEMORADIO THERAPY, IN LOCALLY ADVANCED CERVICAL CANCER: RESULTS FROM THE PHASE 3 INTERNATIONAL, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CALLA TRIAL

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Objectives: In locally-advanced cervical cancer (LACC), platinum-based chemoradiotherapy (CRT) has been the standard-of-care treatment for >20 years. CALLA is the first global Phase 3 study evaluating immune checkpoint inhibition (durvalumab) versus placebo in combination with and following CRT in LACC (NCT03830866).

Methods: Newly-diagnosed, untreated patients with LACC (FIGO 2009 stages IB2–IIB node positive, IIIA–IVA with any node status) were randomized 1:1 to durvalumab (1500 mg IV) or placebo Q4W, for a total of up to 24 months, in combination with and following CRT. CRT comprised concurrent weekly IV cisplatin with EBRT and brachytherapy. RT quality was monitored, with variations evaluated for clinical significance. The primary endpoint is PFS; secondary endpoints include OS, objective response rate, local/distant disease progression incidence, and safety.

Results: 770 patients were randomized (N=385 per arm) at 120 sites in 15 countries. Median age was 49 years; median follow-up was 18.5 months. Durvalumab+CRT did not show a statistically significant improvement in PFS vs placebo+CRT (HR 0.84 [95% CI, 0.65-1.08]; P=0.174); there was no detriment to OS, although data were immature and not formally tested. Adverse events of grade 3–4 occurred in 51.7% and 51.0% of patients in the durvalumab+CRT and placebo+CRT arms, respectively; 12.5% and 9.6% of patients discontinued treatment due to AEs possibly related to study drug.

Conclusions: Durvalumab in combination with and following CRT did not significantly improve PFS in patients with LACC. Safety of durvalumab+CRT was generally comparable to CRT alone, with no new or unexpected toxicity. Funding: AstraZeneca

O002 / #185

Plenary Session

PLENARY 01: OPENING CEREMONY AND ORAL ABSTRACT PRESENTATIONS

29-09-2022 8:00 AM - 10:30 AM

UTERINE TRANSPOSITION: FEASIBILITY STUDY

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Objectives: To evaluate the feasibility of uterine transposition (UT) as a method of preserving ovarian and uterine function after pelvic radiation.

Methods: This was a prospective, non-randomized feasibility study of UT for patients with non-gynecologic pelvic cancers, who require radiation. UT to the upper abdomen was performed 7 to 14 days prior radiation. Frequent clinical examinations and doppler ultrasound were used to evaluate the gonadal vessels vasculature after surgery. The uterus was placed back to the pelvis 2 to 4 weeks after radiation and patients were followed with clinical examinations, pelvic ultrasound and laboratory tests to evaluate hormonal function. Menses were systematically recorded. Cancer treatment and follow-up were performed according to the standard guidelines and no modification were allowed.

Results: From June 2017 to June 2019, eleven patients were selected for the study. Eight patients were submitted to UT (median age of 30.5 yo). There were no transoperative complications. Cervical stenosis was the most common postoperative complication. One patient had uterine necrosis 4 days after surgery, but the right ovary was preserved and kept normal hormonal function. One patient died from carcinomatosis 4 months after UT. All patients who preserved the uterus have normal hormonal levels, menses and sexual activity after treatment. Two patients have had spontaneous pregnancies, one baby was born at 37 weeks and the other patient is 20 weeks pregnant. One patient tried to get pregnant but did not succeed.

Conclusions: Uterine transposition is a feasible procedure to preserve the uterus and gonadal function. Spontaneous and healthy pregnancy is also possible.

O003 / #557

Plenary Session

PLENARY 01: OPENING CEREMONY AND ORAL ABSTRACT PRESENTATIONS

29-09-2022 8:00 AM - 10:30 AM

OVERALL SURVIVAL RESULTS FROM ARIEL3: A PHASE 3 RANDOMIZED, DOUBLE-BLIND STUDY OF RUCAPARIB VS PLACEBO FOLLOWING RESPONSE TO PLATINUM-BASED CHEMOTHERAPY FOR RECURRENT OVARIAN CARCINOMA

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Objectives: In ARIEL3 (NCT01968213), rucaparib maintenance treatment significantly improved progression-free survival (PFS) vs placebo. We present updated PFS2 and preplanned final overall survival (OS) analyses.

Methods: Patients were randomized to receive rucaparib 600 mg BID or placebo. Efficacy was analyzed across the 3 protocol-defined nested cohorts (BRCA-mutant, homologous recombination deficient [HRD], and intent-to-treat [ITT]). PFS2 was an exploratory endpoint, defined as time from randomization to second event of investigator-assessed disease progression, or death due to any cause. OS was a secondary endpoint with analysis planned after 70% of death events. The data cutoff was April 4, 2022, for efficacy and December 31, 2019, for safety. Patients were followed after treatment discontinuation for incidence of myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML); MDS/AML are reported as of April 12, 2022.

Results: Median follow-up was 77.0 months as of the efficacy data cutoff. In the ITT population, death events had occurred in 410/564 (72.7%) patients. PFS2 and OS are presented in the Table. Among placebo-arm patients, ~45% received a PARP inhibitor as a subsequent treatment. Safety was consistent with prior reports; MDS/AML was reported in 14 (3.8%) rucaparib-arm and 6 (3.2%) placebo-arm patients

($P=0.72$) (reported post-study drug treatment in 8 cases in the rucaparib arm and 6 in the placebo arm).

	BRCA		HRD		ITT	
	Rucaparib (n=130)	Placebo (n=66)	Rucaparib (n=236)	Placebo (n=118)	Rucaparib (n=375)	Placebo (n=189)
PFS2 events, n (%)	98 (75.4)	54 (81.8)	183 (77.5)	99 (83.9)	302 (80.5)	162 (85.7)
Median PFS2, months (95% CI)	26.1 (22.8–32.8)	18.4 (15.7–24.4)	24.7 (21.9–26.8)	18.4 (15.8–22.1)	20.6 (18.7–23.5)	16.3 (14.6–17.9)
	HR 0.672 (95% CI 0.480–0.941) $P=0.02$		HR 0.718 (95% CI 0.558–0.923) $P=0.01$		HR 0.703 (95% CI 0.579–0.854) $P<0.01$	
OS events, n (%)	82 (63.1)	48 (72.7)	159 (67.4)	85 (72.0)	270 (72.0)	140 (74.1)
Median OS, months (95% CI)	45.9 (37.7–59.6)	47.8 (43.2–55.8)	40.5 (36.6–48.4)	47.8 (42.7–53.0)	36.0 (32.8–39.4)	43.2 (38.1–46.9)
	HR 0.832 (95% CI 0.581–1.192) $P=0.32$		HR 1.005 (95% CI 0.766–1.320) $P=0.97$		HR 0.995 (95% CI 0.809–1.223) $P=0.96$	

HRs and associated P values were calculated using a stratified log-rank test and stratified Cox-proportional model. P values are nominal with no adjustment for multiplicity.

CI, confidence interval; HR, hazard ratio.

Conclusions: These data support the use of rucaparib as a maintenance treatment for recurrent ovarian carcinoma; although no OS benefit was seen, the PFS benefit for rucaparib was maintained through the subsequent line of therapy.

O004 / #752

Plenary Session

PLENARY 01: OPENING CEREMONY AND ORAL ABSTRACT PRESENTATIONS

29-09-2022 8:00 AM - 10:30 AM

SELECTION CRITERIA FOR OMITTING INTERVAL DEBULKING SURGERY AFTER NEOADJUVANT CHEMOTHERAPY FOR ADVANCED HIGH-GRADE SEROUS CARCINOMA OF THE OVARY: KGOG OVSURG-2016/SCORE STUDY

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Objectives: This study investigates the selection criteria for omitting interval debulking surgery (IDS) after neoadjuvant chemotherapy (NACT) due to a higher response to chemotherapy for advanced ovarian cancer.

Methods: We searched the ovarian, fallopian, or primary peritoneal cancer database registered between January 2000 and May 2021. We included patients with clinical stage III to IV high-grade serous carcinoma of the ovary (HGSC) who received NACT after serial measurement of serum levels of CA-125 regardless of IDS. We calculated the CA-125 ELIMination of Rate Constant K (KELIM) value during two cycles of NACT. Then, we calculated the cut-off values of KELIM for predicting platinum resistance and then evaluated the effect of IDS on progression-free survival (PFS) and overall survival (OS) based on the values.

Results: Among 279 patients, 194 (76%) were treated with NACT/IDS, and 61 (24%) were treated with chemotherapy alone. Although NACT/IDS showed better PFS and OS than chemotherapy alone in patients with lower KELIM (<0.95), no difference in survival was shown in higher KELIM (≥ 0.95 ; Figure 1). In multivariate analysis, IDS was associated with better OS in Low KELIM patients (hazard ratio [HR], 0.517, $p=0.016$), while IDS was not associated with better survival in High KELIM patients (HR, 0.739, $p=0.390$). Also, radiologic complete response (CR) and partial response (PR) were associated with better survival regardless of KELIM score.

Conclusions: In conclusion, for stage III/IV HGSC patients presenting higher KELIM (≥ 0.95), IDS may be omitted when the radiologic CR or PR is accomplished during NACT.

O005 / #638

Plenary Session

PLENARY 01: OPENING CEREMONY AND ORAL ABSTRACT PRESENTATIONS

29-09-2022 8:00 AM - 10:30 AM

PROMISE-2: A ONE STEP DNA-BASED ENDOMETRIAL CANCER MOLECULAR CLASSIFIER

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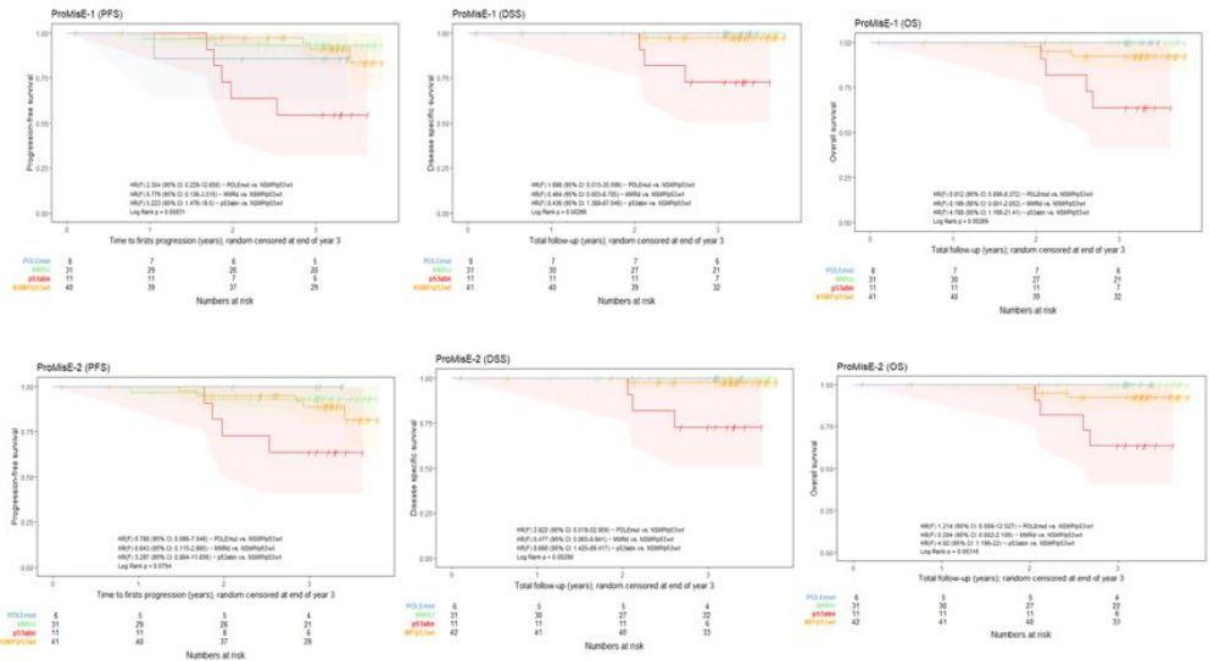
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Objectives: Despite recommendations for the integration of molecular classification in endometrial cancers (EC) into pathology reporting and clinical management, uptake is inconsistent. To assign ProMisE subtype, all molecular components must be available (POLE mutation status, MMR and p53 immunohistochemistry (IHC)) and often components are performed at different stages of care and/or at different centers resulting in diagnostic delays. We assess the performance of a one step DNA-based molecular classifier (ProMisE-2) compared to ProMisE.

Methods: DNA was extracted from ECs that had previously undergone molecular classification using ProMisE (POLE sequencing, IHC for p53 and MMR). ProMisE2 was derived using the Imagia Canexia Health Find It next-generation sequencing assay to assess mutations in POLE, TP53 and presence of microsatellite instability (MSI). Molecular subtypes assigned by ProMisE and ProMisE-2 were assessed for concordance metrics and the ability to recapitulate Kaplan-Meier survival curves.

Results:

Figure 1: Kaplan-Meier survival analyses demonstrating molecular subtype is associated with outcomes across progression free survival, disease specific survival, and overall survival in both ProMisE and ProMisE-2



ProMisE-2 was assessed in 91 ECs with 2 cases failing sequencing coverage thresholds. 85/89 of cases were concordant with a kappa statistic 0.93 and an overall accuracy of 0.96. Five of six cases where ProMisE-2 was performed on matched biopsy and hysterectomy specimens were concordant. Molecular subtype assignment was associated with outcomes (PFS, DSS, OS) in both ProMisE and ProMisE-2 (Figure1).

Conclusions: We demonstrate high concordance of a one step DNA-based EC molecular classifier when compared to the original ProMisE classifier, importantly maintaining the prognostic value of ProMisE and presenting an option for centers where routine MMR and p53 IHC are not performed. Further validation is needed before implementation into clinical practice.

O006 / #1066

Plenary Session

PLENARY 02: ORAL ABSTRACT PRESENTATIONS

29-09-2022 4:55 PM - 5:55 PM

RANDOMIZED TRIAL OF PELVIC RADIATION WITH AND WITHOUT CONCURRENT CISPLATIN IN PATIENTS WITH A PELVIC ONLY RECURRENCE OF ENDOMETRIAL CANCER

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Objectives: The pelvis is a common site of recurrence for patients with endometrial cancers. A randomized trial was conducted to compare progression-free survival in patients treated with radiation therapy alone as compared to radiation therapy with concurrent cisplatin-based chemotherapy.

Methods: 165 Patients were accrued between February 2009 and August 2020. Women with recurrent endometrial carcinoma limited to the pelvis were eligible. The median time for follow up for vital status was 60 months.

Results: Most patients had grade 1 or 2 endometrioid endometrial cancer (81%) and most recurrences were vaginal (86%). Radiation therapy was delivered to the pelvis with 3D or IMRT techniques followed by HDR or LDR interstitial or intracavitary brachytherapy. Chemotherapy was delivered with weekly cisplatin. Grade 4 or higher acute adverse event were reported in 8 participants in the chemotherapy and radiation arm as compared to 1 treated with radiation only. 68% of patients treated with radiation therapy were alive and progression-free as compared to 59.8% of those that received chemotherapy and radiation. Overall, patients treated with weekly cisplatin had a lower rate of PFS as compared to patients treated with radiation alone (stratified HR=1.40, 95% CI: 0.82-2.39, p=0.8919).

Conclusions: Results of this randomized trial suggest that the addition of chemotherapy does not improve, and may worsen, outcomes for patients treated with definitive radiation therapy for recurrent endometrial cancer. Those with low grade and vaginal apex recurrences may be best treated with radiation therapy alone.

O007 / #456

Plenary Session

PLENARY 02: ORAL ABSTRACT PRESENTATIONS

29-09-2022 4:55 PM - 5:55 PM

POST-HOC ANALYSIS OF OBJECTIVE RESPONSE RATE BY MISMATCH REPAIR PROTEIN DIMER LOSS/MUTATION STATUS IN PATIENTS WITH MISMATCH REPAIR DEFICIENT ENDOMETRIAL CANCER TREATED WITH DOSTARLIMAB

Anna Tinker¹, Renaud Sabatier², Adriano Gravina³, Lucy Gilbert⁴, Jubilee Brown⁵, Vanessa Samouëlian⁶, Clare Reade⁷, Cara Mathews⁸, Susan Ellard⁹, Susana Banerjee¹⁰, Maria Pilar Barretina-Ginesta¹¹, Rowan Miller¹², Charles Leath III¹³, Bhavana Pothuri¹⁴, Tao Duan¹⁵, Xinwei Han¹⁶, Eleftherios Zografos¹⁷, Jennifer Veneris¹⁶, Ana Oaknin¹⁸

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Objectives: Mismatch repair (MMR) deficiency is caused by loss of expression of MMR proteins, MLH1, PMS2, MSH2, and/or MSH6, that function as heterodimers (MLH1/PMS2 and MSH2/MSH6) to mediate DNA repair. Loss of function caused by mutation or epigenetic methylation leads to defective MMR and genomic instability. MMR deficient (dMMR) tumors can respond to anti-programmed death 1 (PD-1) therapy. We report on a post-hoc analysis of ORR with loss of MMR dimers and mutation status of MMR genes in patients with dMMR endometrial cancer (EC) treated with dostarlimab.

Methods: GARNET is a multicenter, open-label, single-arm phase 1 study. Cohort A1 enrolled patients with dMMR advanced/recurrent EC. Patients received 500 mg dostarlimab intravenously Q3W for 4 cycles, then 1000 mg Q6W until disease progression, discontinuation, or withdrawal. MMR protein status (presence or loss) was determined by local IHC. MMR gene mutation was determined by Foundation One. MLH1 loss without MMR gene mutation was a surrogate indicator for epigenetic methylation.

Results: Cohort A1 included 143 patients; MMR gene mutation data was available for 101 (Table). Cohort A1 ORR was 45.5%. 66% of patients had loss of MLH1/PMS2; ORR was 48.9%. 11.2% of patients had loss of MSH2/MSH6; ORR was 56.2%. ORR was 41.7% for MLH1 loss with MMR gene mutation and 39.4% for MLH1 loss without MMR gene mutation.

Conclusions: Patients with dMMR advanced/recurrent EC benefitted from dostarlimab, with no noticeable difference by dimer-pair loss or MMR gene methylation/mutation status. These data suggest route to MMR deficiency does not influence response to dostarlimab.

Table

	Patients, N	Responders, n	ORR (%), 95% exact CI
Cohort A1	143	65	45.5 (37.1–54.0)
MLH1/PMS2 loss	94	46	48.9 (38.5–59.5)
MSH2/MSH6 loss	16	9	56.2 (29.9–80.2)
Other ^a	33	10	30.3 (15.6–48.7)
Patients with mutation data	101	—	—
MLH1 loss	78	31	39.7 (28.8–51.5)
MLH1 loss and mutation in MMR gene	12	5	41.7 (15.2–72.3)
MLH1 loss and no mutation in MMR gene	66	26	39.4 (27.6–52.2)

^aOther includes any other pattern of absence of expression of 1 or greater MMR proteins.
MMR, mismatch repair; ORR, objective response rate.

O008 / #283

Plenary Session

PLENARY 02: ORAL ABSTRACT PRESENTATIONS

29-09-2022 4:55 PM - 5:55 PM

COMBINATION THERAPY WITH TOPOTECAN, PACLITAXEL, AND BEVACIZUMAB IMPROVES PROGRESSION-FREE SURVIVAL IN PATIENTS WITH RECURRENT HIGH-GRADE NEUROENDOCRINE CARCINOMA OF THE CERVIX: A NECTUR STUDY

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Objectives: The objective of this study was to evaluate the efficacy of the three-drug regimen topotecan, paclitaxel, and bevacizumab (TPB) in women with recurrent high-grade neuroendocrine cervical cancer (HGNECC).

Methods: This retrospective cohort study used data from the Neuroendocrine Cervical Tumor Registry (NeCTuR). The study compared women with recurrent HGNECC who received TPB as first- or second-line therapy for recurrence and women with recurrent HGNECC who received chemotherapy but not TPB. Progression-free survival from the start of treatment for recurrence to the next recurrence or death, overall survival from first recurrence, and response rates were evaluated.

Results: The study included 57 patients who received TPB as first- or second-line treatment for recurrence and 48 patients who received chemotherapy but not TPB for recurrence. Median progression-free survival was 8.2 months in the TPB group compared to 3.1 months in the non-TPB group, with a hazard ratio for progression of 0.23 (95% CI 0.14-0.40; $P < 0.0001$). In the TPB group, 16% had stable disease, 38% had a partial response, and 16% had a complete response. Significantly more patients in the TPB group than in the non-TPB group remained on treatment at 6 months (67% vs. 25%, $P = 0.0002$) and 1 year (24% vs. 6%, $P = 0.03$). Median overall survival was 16.9 months in the TPB group compared to 14.0 months in the non-TPB group, with a hazard ratio for death of 0.89 (95% CI 0.55-1.45).

Conclusions: TPB is an active regimen in women with recurrent HGNECC and improves progression-free survival while decreasing the hazard ratio for progression.

O009 / #418

Plenary Session

PLENARY 02: ORAL ABSTRACT PRESENTATIONS

29-09-2022 4:55 PM - 5:55 PM

NEXT GENERATION SEQUENCING REVEALS A HIGH PREVALENCE OF PATHOGENIC MUTATIONS IN HOMOLOGOUS RECOMBINATION DNA DAMAGE REPAIR GENES AMONG PATIENTS WITH UTERINE SARCOMA.

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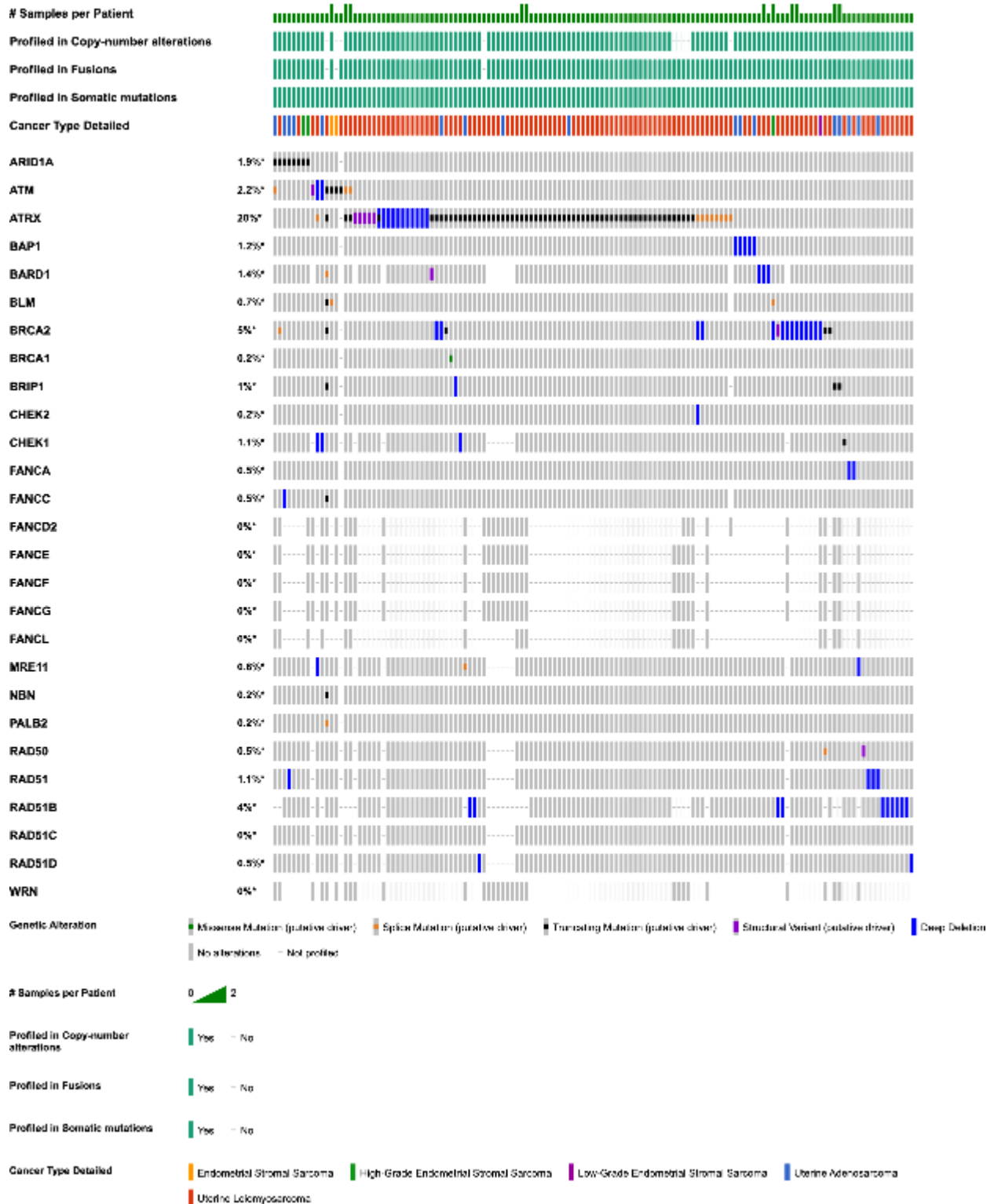
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Objectives: Evaluate the prevalence of alterations in homologous recombination DNA damage repair genes (HR-DDR) among patients with uterine sarcomas.

Methods: The AACR GENIE v12.0 database was accessed and patients with uterine leiomyosarcoma, adenocarcinoma and endometrial stromal sarcoma were identified. We examined the incidence of pathogenic alterations of genes involved in HR-DDR: ATM, ARID1A, ATRX, BAP1, BARD1, BLM, BRCA2, BRCA1, BRIP1, CHEK2, CHEK1, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL, MRE11, NBN, PALB2, RAD50, RAD51, RAD51B, RAD51C, RAD51D, WRN.

Results: A total of 433 patients contributing to 450 samples were identified; 298 patients with leiomyosarcoma (LMS), 53 patients with adenocarcinoma (AS), 30 patients with low-grade endometrial stromal sarcoma (ESS), 19 patients with high-grade, and 34 patients with ESS not specified (34 samples). The overall incidence of pathogenic HR-DDR gene alterations was 30% (135/450). The most prevalent gene alteration was ATRX (20%, 84/419) followed by BRCA2 (5%, 20/416), RAD51B (4%, 10/271), ATM (2.2%, 10/446) and ARID1A (1.9%, 8/419). The highest incidence of HR-DDR gene alterations was observed in leiomyosarcoma (36.5%) followed by adenocarcinoma (29.8%), and HG-ESS (26.3%) while HR-DDR gene alterations were less common in ESS NOS (17.7%) and LG-ESS (13.3%). In the present cohort, incidence of TP53 mutations was 49% (213/432), while other common pathogenic gene alterations included the RB1 (29%, 128/449), PTEN (13%, 58/449) and MED12 (11%, 42/375)

genes.



Conclusions: Approximately 1 in 3 patients with uterine sarcoma, harbor a pathogenic alteration in HR-DDR genes. These results provide further rationale for the design of molecularly driven clinical trials exploring agents targeting DNA damage repair.

O010 / #851

Plenary Session

PLENARY 05: ORAL ABSTRACT PRESENTATIONS & CLOSING CEREMONY

01-10-2022 3:55 PM - 5:25 PM

IMPACT OF COMORBIDITIES, POSTOPERATIVE COMPLICATIONS AND CENTER VOLUME ON OVERALL SURVIVAL IN A REAL-LIFE COHORT OF 29,879 OVARIAN CANCER PATIENTS

Floriane Jochum¹, Anne-Sophie Hamy², Enora Laas¹, Elise Dumas³, Eric Daoud³, Aryn Kassara³, Paul Gougis³, Thomas Gaillard¹, Lise Lecointre⁴, Cherif Akladios⁴, Fabrice Lecuru¹, Fabien Reyat¹

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Objectives: The primary objective of this study was to analyze the impact of comorbidities, postoperative complications and center volume on overall survival in a real-life cohort of ovarian cancer patients in France.

Methods: All French women aged 18 years or over, with ovarian cancer newly diagnosed between January 2013 and December 2019, registered in the general health insurance coverage plan were included in the cohort. Ovarian cancer treatments, comorbidities, postoperative complications and death were extracted from hospital discharge reports. The characteristics of the centers were also collected.

Results: We included 29,879 patients with ovarian cancer in the cohort. The median age was 66 [57-74] years, and 24,783 (82.9%) presented an advanced stage at diagnosis (FIGO IIB-IVB). A total of 16,048 (53.7%) patients had at least one comorbidity at the time of diagnosis, mainly hypertension (n=6,800) and obesity (n=2,505). Patients received primary surgery, interval surgery, or chemotherapy alone in 31.5%, 30.4%, and 38.1% of cases, respectively. A total of 3,031 (16.1%) patients presented a postoperative complication Clavien-Dindo III or more within 90 days of cytoreduction surgery, mainly digestive (60.4%). For advanced stages, the median overall survival was 47 [45.9-48] months. The number of comorbidities, the occurrence of a complication and low center volume had a significant negative impact on the overall survival.

Conclusions: Real-life data give the opportunity to study the key health indicators in ovarian cancer. A personalized care pathway should be a priority for patients with comorbidities and at risk of postoperative complications.

O011 / #496

Plenary Session

PLENARY 05: ORAL ABSTRACT PRESENTATIONS & CLOSING CEREMONY

01-10-2022 3:55 PM - 5:25 PM

MIRVETUXIMAB SORAVTANSINE AND BEVACIZUMAB IN FOLATE RECEPTOR ALPHA-POSITIVE OVARIAN CANCER: EFFICACY IN PATIENTS WITH AND WITHOUT PRIOR BEVACIZUMAB

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Objectives: Mirvetuximab soravtansine (MIRV) is a first-in-class ADC comprising a folate receptor- α (FR α)-binding antibody, cleavable linker, and maytansinoid DM4 payload. As part of the phase 1b/2 trial (NCT02606305), efficacy, safety, and tolerability of MIRV and bevacizumab (BEV) were evaluated in patients with recurrent FR α -positive ovarian cancer (OC) measured by immunohistochemistry (PS2+ \geq 25%).

Methods: Patients received MIRV (6 mg/kg, adjusted ideal body weight) and BEV (15 mg/kg) intravenously on Day 1 of a 3-week cycle. Primary endpoint was confirmed ORR assessed by RECIST v1.1. Safety and tolerability of MIRV + BEV were secondary endpoints.

Results: Patients enrolled (N=126; median age 62 years) were heavily pretreated (46%, \geq 3 prior therapies) and 75% were platinum resistant. Prior taxane, BEV, or PARPi treatment occurred in 98%, 52%, and 27%, respectively. Low, medium, and high FR α expression in patient tumors was 10%, 40%, and 49%, respectively. MIRV demonstrated anti-tumor activity in the entire cohort (ORR 44%, mDOR 11.8 months, mPFS 8.2 months), with ORR of 58% in BEV-naïve and 32% in prior BEV (Table 1). Grade 3+ treatment emergent adverse events (TEAEs) were low; common TEAEs (Grade 3+, all grade) included diarrhea (2%, 67%), nausea (2%, 59%), blurred vision (1%, 56%), fatigue (5%, 53%), and hypertension (17%),

33%).

Table 1. Efficacy of patients treated with MIRV + BEV with no prior or prior exposure to BEV.

	ORR, % (95% CI)	mDOR, mo (95% CI)	mPFS, mo (95% CI)
Total population (N=126)	44 (35.6, 53.6)	11.8 (8.3, 13.7)	8.2 (6.8, 9.9)
No prior BEV (n=60)	58 (44.9, 70.9)	11.8 (8.3, 12.9)	9.7 (8.2, 13.2)
Prior BEV (n=66)	32 (20.9, 44.4)	9.7 (4.9, 15.7)	6.8 (5.5, 8.2)

Conclusions: MIRV and BEV demonstrated anti-tumor activity, regardless of prior BEV treatment, and should be considered in FR α -positive recurrent OC. A randomized phase 3 trial (GLORIOSA) will evaluate MIRV and BEV in the maintenance setting in patients with FR α -high platinum-sensitive OC.

O012 / #352

Plenary Session

PLENARY 05: ORAL ABSTRACT PRESENTATIONS & CLOSING CEREMONY

01-10-2022 3:55 PM - 5:25 PM

ATEZOLIZUMAB AND BEVACIZUMAB IN RECURRENT ENDOMETRIAL CANCER: A PHASE II, MULTI INSTITUTIONAL TRIAL

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Objectives: Clinical data across several solid tumors, including EC, suggests synergy between immune checkpoint inhibition and anti-angiogenic agents. This study sought to evaluate the efficacy and safety of Atezolizumab (A) and Bevacizumab (Bev) in recurrent EC.

Methods: This multicenter, single arm trial (NCT03526432) enrolled patients with recurrent EC (1-2 priors) to receive A 1,200mg and Bev 15 mg/kg day 1 every 21 days. The primary endpoint was overall response rate (ORR) and duration of response (DOR).

Results: There were 57 response evaluable patients who received both drugs for the first two cycles. Median age was 65 (25-91) years and race included 22.8% Black and 2% American Indian. 61% had endometrioid tumors, 18% UPSC or carcinosarcoma each and 4% clear cell. 87% were mismatch repair proficient (MMRp) and 13% MMRd. 15% had prior pelvic radiation. Adverse events and clinical activity in Table 1. Translational data including blood immune cell population analysis by CyTOF will be presented with the clinical data.

Conclusions: The ORR for A and Bev approximates that seen with Len/Pem with far fewer side effects. An ongoing trial within the Alliance contains this similar arm and if confirmatory would support this combination as a treatment option.

Total Number of Subjects	57
Adverse events	n (%)
Grade 3 due to atezolizumab	4 (7%)
Grade 3 due to bevacizumab	12 (22%)
Grade 4	0
Dose interruption	45 (79%)
Dose reduction	2 (4%)
Discontinued due to toxicity	9 (16%)
Clinical Activity	
ORR for all	30% (95% CI 18-43)
ORR for MMRp	33% (95% CI 20-48)
Median DOR (months)	15 (95% CI 2.9-34)
Median PFS (months)	7.87 (95% CI 5.5-11.7)

O013 / #813

Plenary Session

PLENARY 05: ORAL ABSTRACT PRESENTATIONS & CLOSING CEREMONY

01-10-2022 3:55 PM - 5:25 PM

TRENDS OF METASTATIC LEIOMYOSARCOMA FOLLOWING THE US FOOD AND DRUG ADMINISTRATION (FDA) WARNING ON LAPAROSCOPIC POWER MORCELLATORS

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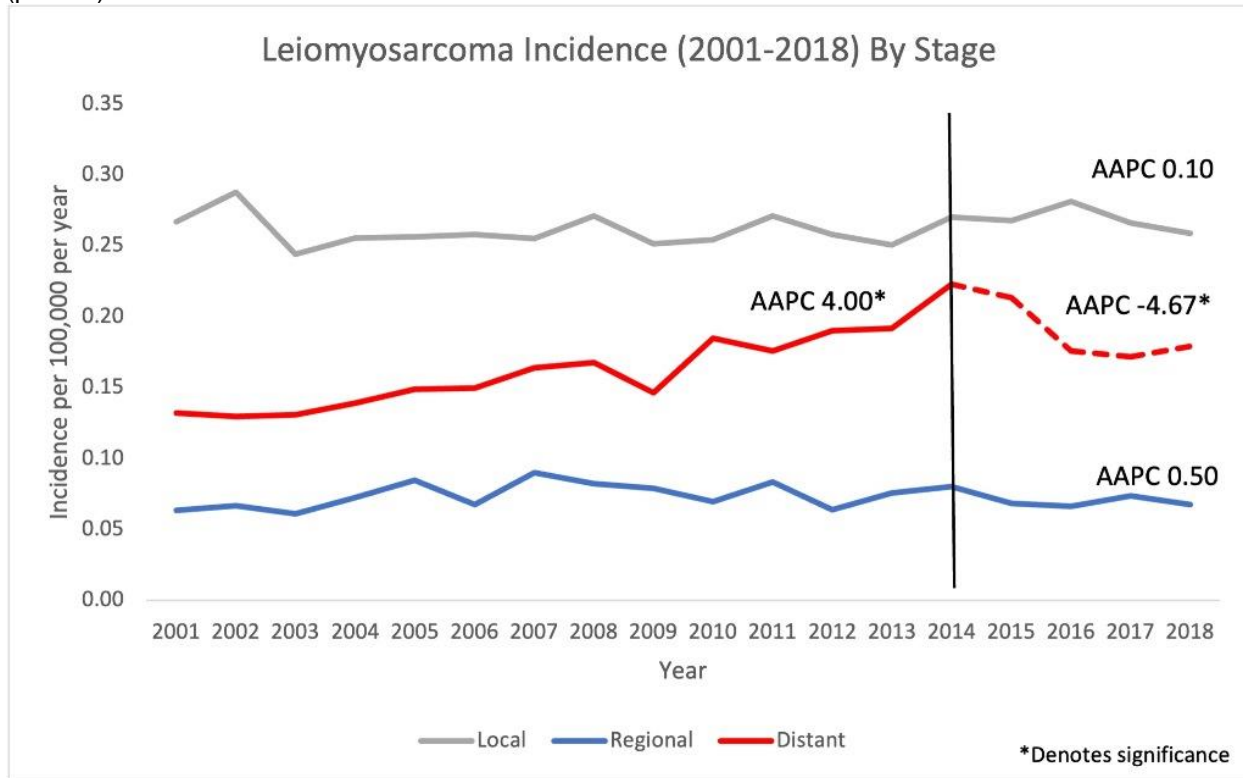
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Objectives: In 2014, the FDA released a warning against the use of laparoscopic power morcellators in women undergoing myomectomy or hysterectomy for the treatment of uterine fibroids due to the risk of spreading unsuspected leiomyosarcoma. We proposed to describe the pattern of incidence and survival of leiomyosarcoma (LMS) before and after the FDA warning.

Methods: Incidence data were obtained from the United States Cancer Statistics (USCS) database from 2001-2018 and survival data were obtained from the National Cancer Database (NCDB) for diagnoses made between 2004-2016. Average annual percent change (AAPC) was calculated using Joinpoint regression.

Results: Using USCS data from 2001 to 2018, 16,808 cases of leiomyosarcoma were diagnosed (10,207 (60.7%) White, 3,773 (22.4%) Black, 1,924 (11.4%) Hispanic, 727 (4.3%) Asian/Pacific Islander). Prior to the FDA warning, from 2001 to 2014, the incidence of distant LMS increased 4.00% annually ($p < 0.05$). After the FDA warning, from 2014 to 2018, the incidence of distant LMS decreased 4.67% annually ($p < 0.05$). However, the incidence of local and regional LMS remained stable from 2001 to 2018 (AAPC 0.10 and 0.50 respectively, $p > 0.05$). Using NCDB data, we divided the study group into diagnoses made during 3 time periods (2004-2007, 2008-2012, 2013-2016). The LMS 5-year survival rate remained unchanged at 36.62%, 36.77% and 36.46% respectively

($p > 0.05$).



Conclusions: Since the FDA warning of the power morcellator in 2014, distant LMS has decreased 4.67% per year. The correlation of these findings to the FDA warning of power morcellators warrants further investigation.

O014 / #415

Plenary Session

PLENARY 05: ORAL ABSTRACT PRESENTATIONS & CLOSING CEREMONY

01-10-2022 3:55 PM - 5:25 PM

PHASE II TRIAL OF PEMBROLIZUMAB AND EPACADOSTAT IN RECURRENT CLEAR CELL CARCINOMA OF THE OVARY: AN NRG ONCOLOGY STUDY

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Objectives: Early reports of PD-1 inhibition in ovarian clear cell carcinomas demonstrate promising durable response. We evaluated the combination of pembrolizumab and IDO-1 inhibitor epacadostat in patients with recurrent ovarian clear cell carcinomas.

Methods: This single arm, two-stage, phase 2 trial included those with measurable disease and 1-3 prior regimens. Patients received intravenous pembrolizumab 200 mg every 3 weeks and epacadostat orally 100 mg twice a day. Primary endpoint was overall response rate (ORR), with secondary endpoints of toxicity, progression-free survival (PFS) and overall survival (OS).

Results: Between September 28, 2018 and April 10, 2019, 14 patients accrued at first stage. Rate of accrual was 2.3 patients per month, higher than estimated. Median age was 65 (44-89), 10 (71.4%) had ≥ 2 prior regimens. ORR was 21% (95% CI 5-51%) within 7 months of study entry with 3 partial responses, 4 had stable disease for disease control rate of 50%. Median PFS was 4.8 months (95% CI: 1.9-9.6), OS 18.9 months (95% CI: 1.9-NR). Most common grade ≥ 3 adverse events reported were electrolyte changes and bowel obstruction. In July 2019, the study reached the pre-specified criteria to re-open to second stage, however after holding for amendment, the study closed prematurely in February 2021 due to insufficient drug supply.

Conclusions: Combination of pembrolizumab and epacadostat demonstrated an ORR of 21% in this small cohort of recurrent ovarian clear cell carcinomas. The rapid rate of accrual highlights the enthusiasm and need for therapeutic studies in patients with ovarian clear cell carcinomas.

O015 / #502

Plenary Session

PLENARY 05: ORAL ABSTRACT PRESENTATIONS & CLOSING CEREMONY

01-10-2022 3:55 PM - 5:25 PM

MOLECULAR STRATIFICATION OF OVARIAN CLEAR CELL CARCINOMA PREDICTS CLINICAL OUTCOMES

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Objectives: We sought to investigate if molecular profiles and endometrial cancer (EC)-based molecular subtyping are associated with clinicopathologic variables and outcomes in ovarian clear cell carcinomas (OCCCs).

Methods: Patients with OCCC who underwent clinical panel-based sequencing from 4/2015-1/2021 were identified. Pathogenic somatic alterations, EC molecular subtypes, clinicopathologic variables, and survival outcomes were obtained. Appropriate statistical methods were applied.

Results: Following central pathology review, 119 OCCCs were identified. Stage at diagnosis was equally distributed (54% I/II; 46% III/IV). Eighty-three percent (n=99) were copy number (CN)-low, 12% (n=14) were CN-high, 4% (n=5) were microsatellite instability (MSI)-high, and 1% (n=1) were POLE mutated. The most frequent genetic alterations were ARID1A (n=80, 67%), PIK3CA (n=56, 47%), TERT promoter (n=27, 23%), and PPP2R1A (n=19, 16%). ARID1A and TERT alterations were mutually exclusive (p=0.04, q=0.19). Endometriosis was significantly enriched in CN-low OCCCs (p=0.02), and patients diagnosed at <50 years of age were more likely to harbor PIK3CA alterations (p=0.04). In the entire cohort, multivariate analysis of outcome revealed that Asian race (p=0.04), advanced stage (p<0.01), and CN-high subtype (p=0.03) were significantly associated with worse progression-free survival; advanced stage (p=0.01) and PPP2R1A alterations (p=0.04) were significantly associated with worse overall survival. Univariate sensitivity analysis including only patients who had the initial treatment planning at our institution found the same survival associations.

Conclusions: OCCC is a heterogenous group of tumors with varied clinical outcomes and molecular profiles. In this retrospective series of OCCCs, race, EC-based molecular subtype, stage at diagnosis, and PPP2R1A alterations were predictive of outcome.

O016 / #739

Plenary Session

PLENARY 05: ORAL ABSTRACT PRESENTATIONS & CLOSING CEREMONY

01-10-2022 3:55 PM - 5:25 PM

OUTCOMES OF GYNAECOLOGICAL CANCER SURGERY DURING THE COVID-19 PANDEMIC: RESULTS FROM THE INTERNATIONAL, MULTICENTER, PROSPECTIVE COVIDSURG-GYNAECOLOGICAL CANCER STUDY.

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Objectives: The magnitude of adverse outcomes caused by the disrupted surgical cancer care during the COVID-19 pandemic is unclear. Our aim was to evaluate the changes in care and short-term outcomes of surgical patients with gynecological cancers during the initial phase of the COVID-19 pandemic internationally.

Methods: A multicenter, international prospective cohort study including consecutive patients with gynecological cancers who were initially planned for non-palliative surgery. Primary outcome: 30-day postoperative SARS-CoV-2 infection rate. Secondary outcomes: 30-day perioperative mortality and morbidity, COVID-19-related treatment modifications.

Results: We included 3973 patients (52 countries; 7 world regions). Lower-than-reported rate (22/3778; 0.6%) of perioperative SARS-CoV-2 infections was observed. This group had higher morbidity (63.6% vs 19.1%; $p < 0.0001$) and mortality (18.2% vs 0.7%; $p < 0.0001$), compared to the uninfected cohort. In 20.7% (823/3973), standard of care was adjusted. Significant delay (>8 weeks) was observed in 11.2% (424/3784), particularly in those with ovarian cancer (213/1355; 15.7%). This delay was associated with a composite of adverse outcomes including disease progression and death (95/424; 22.4% versus 601/3360; 17.9%, $p = 0.024$), compared to those who had operations within 8 weeks of their MDT decisions. One in thirteen did not receive their planned operations (189/2430; 7.9%), in whom 1 in 20 (5/189; 2.7%) died and 1 in 5 (34/189; 18%) experienced disease progression or death within 3 months of decisions for surgery.

Conclusions: One in five surgical patients with gynecological cancer worldwide experienced management modifications during the COVID-19 pandemic. Significant adverse outcomes were observed in those with delayed or cancelled operations- coordinated mitigating strategies are urgently needed.