

OP005/#352

SAFETY OF VAGINAL HYSTERECTOMY FOR CERVICAL CANCER: A MULTICENTER COHORT STUDY ON BEHALF OF THE 4C (CANADIAN CERVICAL CANCER COLLABORATIVE) WORKING GROUP

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Objectives Inferior outcomes of minimally invasive surgery (MIS) in cervical cancer may be attributable to exposure of peritoneum to tumor at colpotomy. Vaginal surgery may minimize surgical morbidity while avoiding dissemination. We sought to compare cervical cancer outcomes by surgical approach.

Methods A retrospective cohort study of cervical cancer patients in ten Canadian centers between 2007–2017. Patients with FIGO 2018 stage IA1, LVI+, and stages IA2-IIIc tumors <4cm were included. Patients undergoing MIS, abdominal (AH) and vaginal or laparoscopy-assisted vaginal hysterectomy (CLVH) were compared. PFS and OS were assessed using the product-limit method, and Cox regression was performed to evaluate association of surgery with outcomes.

Results 1066 patients met inclusion criteria (518 MIS, 436 AH and 110 CLVH). Radical hysterectomy was performed in 80% (CLVH), 96.9% (MIS) and 89.8% (AH) of cases. CLVH cases included more adeno/adenosquamous cancers (70.9% vs. 38.3% (MIS) and 50%(AH), $p<0.001$), more microinvasive disease (30.9% vs 21.4%(MIS) and 15.8%(AH), $p=0.005$), smaller tumors (8mm vs. 13mm(MIS), 15mm(AH), $p=0.006$), fewer LVI+ (20.9% vs. 39%(MIS), 35.9%(AH), $p=0.001$) and similar rates of lymphatic spread (11.1% vs 11.1%(MIS), 9.7%(AH)). CLVH was associated with fewer intraoperative (5.6% vs 5.6% (MIS), 10.1%(AH), $p=0.023$) and postoperative (11.8% vs 18.9%(MIS), 24.5%(AH), $p=0.006$) complications and readmissions (4.6% vs. 11.9%(MIS), 13.9%(AH), $p=0.028$). CLVH was further associated with a lower risk of recurrence, even when adjusted for age and stage (HR=2.6, 95% CI 1.04–6.51 (AH) and HR=3.07, 95% CI 1.23–7.64 (MIS)).

Conclusions CLVH for cervical cancer is associated with excellent perioperative outcomes. Oncological outcomes appear promising and warrant prospective exploration.

OP006/#489

SURVIVAL IMPACT OF ONTOGENETIC SURGERY FOR NEWLY DIAGNOSED CERVICAL CANCER

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Objectives To evaluate the survival impact of ontogenetic surgery for stage IB1-IVB cervical cancer.

Methods We prospectively enrolled patients with stage IB1-IVB cervical cancer (NCT02986568) for patients treated with total mesometrial resection (TMMR) or laterally extended endopelvic resection (LEER) from 2016 to 2020, who received adjuvant chemotherapy if resection margin was positive or positive pelvic lymph nodes ≥ 2 or positive para-aortic lymph node metastasis. For historical comparison, a retrospective cohort of patients who underwent standard treatment was gathered from 2010 to 2020. Clinico-pathologic characteristics, progression-free survival (PFS), and overall survival (OS) were compared between the prospective and retrospective cohorts.

Results A total of 46 patients underwent TMMR or LEER in the prospective cohort and 207 patients received standard treatment in the retrospective cohort. Clinico-pathologic characteristics were equally balanced in both cohorts. In terms of survival analysis, ontogenetic surgery showed worse PFS (mean, 53.08 vs 88.3 mons, $p=0.003$) and no differences in OS. In subgroup analysis, stage IB1-IIA2 patients did not show differences in survival, whereas stage IIB-IVB patients showed worse PFS (mean, 30.9 vs. 40.3 mons, $p=0.015$) and no difference in OS. In multivariate analysis, ontogenetic surgery was associated with an increase of recurrence (HR, 3.55; 95% CI, 1.34–9.39)

Conclusions Ontogenetic surgery was associated with increased recurrence in locally advanced cervical cancer despite its similar efficacy to standard treatment in early-stage disease. Thus, we have stopped the recruitment of patients with locally advanced cervical cancer for ontogenetic surgery for considering this harmful effect.

OP007/#276

PHASE I STUDY OF MIRVETUXIMAB SORAVTANSINE (MIRV) AND RUCAPARIB FOR RECURRENT ENDOMETRIAL, OVARIAN, FALLOPIAN TUBE OR PRIMARY PERITONEAL CANCER

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Objectives To estimate the maximally tolerated dose (MTD) and toxicities associated with MIRV and rucaparib.

Methods Patients had to be folate receptor α (FR α) positive by IHC ($\geq 25\%$ of tumor staining at $\geq 2+$ intensity). Using a 3+3 design patients received MIRV (4–6 mg/kg IV every 3 weeks) and rucaparib PO BID (400–600 mg) depending on the dose level.

Results >100 patients were screened for FR α expression; 21 have been enrolled, 16 with ovarian and 5 with endometrial cancer. Median age was 64.5, with 3 (range 1–9) prior lines of treatment. 6 patients completed DL2 (5/500), however, 2 DLTs (grade 3 fatigue), let us to establish the RP2d at DL1 (MIRV 5 mg/kg IV every 3 weeks and rucaparib 400 mg PO BID). Treatment related toxicities (all grades) occurring in $\geq 25\%$ of patients included fatigue (73%), nausea (67%), blurred vision (60%), anemia (47%), anorexia (47%), mucositis (40%), ALT/AST elevated (40%), dry eyes (33%), vomiting (27%), thrombocytopenia (27%), weight loss (27%), leukopenia (27%), dysgeusia (27%). Grade ≥ 3 toxicities were fatigue

Abstracts

(20%), pneumonitis (13%), anemia (13%), diarrhea (7%), cataract (7%), lymphopenia (7%), thrombocytopenia (7%), weight loss (7%), hypokalemia (7%). Sixteen patients are currently evaluable for response; 6 (37.5%) with PR, 8 (50%) SD, 2 (12.5%) PD; ORR 33% (4/12) in ovarian cancer and 50% (2/4) in endometrial cancer. Median PFS is 6.3 months with 95%CI (0.7, 13.8) months.

Conclusions Combination rucaparib and MIRV was tolerable with mostly manageable side effects and encouraging activity in this heavily pretreated population (including prior PARPi) of both endometrial and ovarian cancer.

OP008/#194

P53ABN MOLECULAR SUBTYPE ENCOMPASSES A MORPHOLOGICALLY DIVERSE SUBSET OF ENDOMETRIAL CANCERS AND IDENTIFIES THERAPEUTIC OPPORTUNITIES TO IMPROVE OUTCOMES

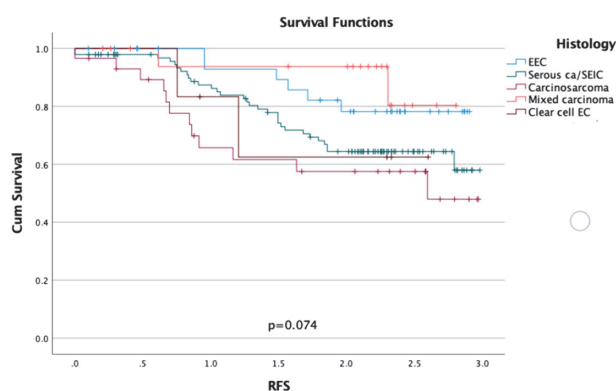
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Objectives Molecular classification of endometrial cancer (EC) has important prognostic and therapeutic implications. p53abn EC represent the most aggressive molecular subtype, and recent data has shown a survival benefit from chemotherapy and targeted therapies. We describe the clinicopathologic diversity in presentation and outcomes of p53abn ECs.

Methods Molecular classification was performed on ECs diagnosed in 2016 from 30 Canadian centres. Clinicopathologic and outcome data were collected.

Results 190 ECs were p53abn subtype; 100 serous, 33 endometrioid, 29 carcinosarcomas, 20 mixed, 6 clear cell carcinoma, 2 undifferentiated. 13 p53abn endometrioid ECs were low grade (Gr1/2). There was a trend for worse outcomes



Abstract OP008/#194 Figure 1

with non-endometrioid histotypes($p=0.074$). Non-endometrioid p53abn ECs were more likely to present with advanced stage (III-IV) disease compared to endometrioid p53abn ECs (43% vs 15%, $p=0.003$). There was significant variation in adjuvant treatment; 28% patients received no adjuvant therapy, 40% received no chemotherapy. of the patients who had no chemotherapy, 20/76 (26.3%) had a disease related event (progression/disease specific death). Stage I p53abn low grade ECs had worse outcomes (5-fold) than stage I low grade ECs of all other molecular subtypes combined.

Conclusions p53abn EC was observed across a range of histotypes including low grade ECs, with no significant difference in outcomes based on histotype. EC risk stratification based on histotype and stage failed to identify 25% of patients as high risk and 15% as intermediate risk based on the 2020 ESGO/ESTRO/ESP EC guidelines, which resulted in a missed opportunity for chemotherapy and targeted therapy.

OP009/#222

COMBINED ORAL MEGESTROL ACETATE/LEVONORGESTREL-INTRAUTERINE SYSTEM FOR ATYPICAL ENDOMETRIAL HYPERPLASIA: A SINGLE-CENTER PROSPECTIVE RANDOMIZED CONTROLLED PILOT STUDY

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Objectives To assess if addition of levonorgestrel-intrauterine system (LNG-IUS) to megestrol acetate (MA) could improve treatment outcomes for patients with atypical endometrial hyperplasia (AEH).

Methods In this open-label randomized controlled pilot study, patients were recruited from the Obstetrics and Gynecology Hospital, Fudan University. Between June, 2017, and June, 2020, 180 AEH patients met inclusion criteria and were randomly assigned (1:1:1) to MA+LNG-IUS group (160mg oral MA daily with LNG-IUS), LNG-IUS group or MA group (160mg oral MA daily). Hysteroscopic pathological evaluation was performed every 3 months during the treatment duration. The primary outcome, time to complete response (CR), was time from treatment initiation to pathologic assessments without lesions. Efficacy and safety were assessed in patients who received treatment. ClinicalTrials.gov: NCT03241888.

Results Median age was 33 years (range 19–44). 58 received MA, 59 received LNG-IUS and 54 received MA+LNG-IUS. At data cutoff of the analysis on January 31, 2021, median follow-up was 25.9 months (range, 2.8–43.5). CR time was significantly shorter with LNG-IUS compared with MA (median, 4.4 vs. 7.0 months; hazard ratio 1.53; 95% confidence interval, 1.05–2.25; $p=0.028$). No significant difference in CR time was found between MA+LNG-IUS group and MA group. LNG-IUS group had lower incidence of weight gain ($p<0.001$), abdominal pain ($p=0.036$), insomnia ($p=0.005$), edema face ($p=0.003$), night sweats ($p=0.003$) and nocturia ($p=0.002$) than MA group. MA+LNG-IUS group had higher incidence of vaginal hemorrhage ($p=0.002$) than MA group.

Conclusions LNG-IUS significantly improved CR time compared with that for MA, with less adverse events, and might be an alternative treatment option for AEH patients.