GINECOLOGÍA

➢ ConCerv: a prospective trial of conservative surgery for low-risk early-stage cervical cancer

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ABSTRACTO: Objective: The objective of the ConCerv Trial was to prospectively evaluate the feasibility of conservative surgery in women with early-stage, low-risk cervical cancer. Methods: From April 2010 to March 2019, a prospective, single-arm, multicenter study evaluated conservative surgery in participants from 16 sites in nine countries. Eligibility criteria included: (1) FIGO 2009 stage IA2-IB1 cervical carcinoma; (2) squamous cell (any grade) or adenocarcinoma (grade 1 or 2 only) histology; (3) tumor size <2 cm; (4) no lymphovascular space invasion; (5) depth of invasion <10 mm; (6) negative imaging for metastatic disease; and (7) negative conization margins. Cervical conization was performed to determine eligibility, with one repeat cone permitted. Eligible women desiring fertility preservation underwent a second surgery with pelvic lymph node assessment, consisting of sentinel lymph node biopsy and/or full pelvic lymph node dissection. Those not desiring fertility preservation underwent simple hysterectomy with lymph node assessment. Women who had undergone an 'inadvertent' simple hysterectomy with an unexpected post-operative diagnosis of cancer were also eligible if they met the above inclusion criteria and underwent a second surgery with pelvic lymph node dissection only. Results: 100 evaluable patients were enrolled. Median age at surgery was 38 years (range 23-67). Stage was IA2 (33%) and IB1 (67%). Surgery included conization followed by lymph node assessment in 44 women, conization followed by simple hysterectomy with lymph node assessment in 40 women, and inadvertent simple hysterectomy followed by lymph node dissection in 16 women. Positive lymph nodes were noted in 5 patients (5%). Residual disease in the post-conization hysterectomy specimen was noted in 1/40 patients-that is, an immediate failure rate of 2.5%. Median follow-up was 36.3 months (range 0.0-68.3). Three patients developed recurrent disease within 2 years of surgery-that is, a cumulative incidence of 3.5% (95% CI 0.9% to 9.0%). Discussion: Our prospective data show that select patients with early-stage, low-risk cervical carcinoma may be offered conservative surgery.

➢ Pembrolizumab for Persistent, Recurrent, or Metastatic Cervical Cancer

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ABSTRACTO: Background: Pembrolizumab has efficacy in programmed death ligand 1 (PD-L1)-positive metastatic or unresectable cervical cancer that has progressed during chemotherapy. We assessed the relative benefit of adding pembrolizumab to chemotherapy with or without bevacizumab. Methods: In a double-blind, phase 3 trial, we randomly assigned patients with persistent, recurrent, or metastatic cervical cancer in a 1:1 ratio to receive pembrolizumab (200 mg) or placebo every 3 weeks for up to 35 cycles plus platinum-based chemotherapy and, per investigator discretion, bevacizumab. The dual primary end points were progression-free survival and overall survival, each tested sequentially in patients with a PD-L1 combined positive score of 1 or more, in the intention-to-treat population, and in patients with a PD-L1 combined positive score of 10 or more. The combined positive score is defined as the number of PD-L1-staining cells divided by the total number of viable tumor cells, multiplied by 100. All results are from the protocol-specified first interim analysis. Results: In 548 patients with a PD-L1 combined positive score of 1 or more, median progression-free survival was 10.4 months in the pembrolizumab group and 8.2 months in the placebo group (hazard ratio for disease progression or death, 0.62; 95% confidence interval [CI], 0.50 to 0.77; P<0.001). In 617 patients in the intention-to-treat population, progression-free survival was 10.4 months and 8.2 months, respectively (hazard ratio, 0.65; 95% CI, 0.53 to 0.79; P<0.001). In 317 patients with a PD-L1 combined positive score of 10 or more, progression-free survival was 10.4 months and 8.1 months, respectively (hazard ratio, 0.58; 95% CI, 0.44 to 0.77; P<0.001). Overall survival at 24 months was 53.0% in the pembrolizumab group and 41.7% in the placebo group (hazard ratio for death, 0.64; 95% CI, 0.50 to 0.81; P<0.001), 50.4% and 40.4% (hazard ratio, 0.67; 95% CI, 0.54 to 0.84; P<0.001), and 54.4% and 44.6% (hazard ratio, 0.61; 95% CI, 0.44 to 0.84; P = 0.001), respectively. The most common grade 3 to 5 adverse events were anemia (30.3% in the pembrolizumab group and 26.9% in the placebo group) and neutropenia (12.4% and 9.7%, respectively). Conclusions: Progression-free and overall survival were significantly longer with pembrolizumab than with placebo among patients with persistent, recurrent, or metastatic cervical cancer who were also receiving chemotherapy with or without bevacizumab.

- **The annual recurrence risk model for tailored surveillance strategy in patients with cervical cancer**

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ABSTRACTO: Purpose: Current guidelines for surveillance strategy in cervical cancer are rigid, recommending the same strategy for all survivors. The aim of this study was to develop a robust model allowing for individualised surveillance based on a patient's risk profile. Methods: Data of 4343 early-stage patients with cervical cancer treated between 2007 and 2016 were obtained from the international SCCAN (Surveillance in Cervical Cancer) consortium. The Cox

proportional hazards model predicting disease-free survival (DFS) was developed and internally validated. The risk score, derived from regression coefficients of the model, stratified the cohort into significantly distinctive risk groups. On its basis, the annual recurrence risk model (ARRM) was calculated. Results: Five variables were included in the prognostic model: maximal pathologic tumour diameter; tumour histotype; grade; number of positive pelvic lymph nodes; and lymphovascular space invasion. Five risk groups significantly differing in prognosis were identified with a five-year DFS of 97.5%, 94.7%, 85.2% and 63.3% in increasing risk groups, whereas a two-year DFS in the highest risk group equalled 15.4%. Based on the ARRM, the annual recurrence risk in the lowest risk group was below 1% since the beginning of follow-up and declined below 1% at years three, four and >5 in the medium-risk groups. In the whole cohort, 26% of recurrences appeared at the first year of the follow-up, 48% by year two and 78% by year five. Conclusion: The ARRM represents a potent tool for tailoring the surveillance strategy in early-stage patients with cervical cancer based on the patient's risk status and respective annual recurrence risk. It can easily be used in routine clinical settings internationally.

➢ Post-recurrence survival in patients with cervical cancer

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ABSTRACTO: Background: Up to 26% of patients with early-stage cervical cancer experience relapse after primary surgery. However, little is known about which factors influence prognosis following disease recurrence. Therefore, our aims were to determine post-recurrence disease-specific survival (PR-DSS) and to identify respective prognostic factors for PR-DSS. Methods: Data from 528 patients with early-stage cervical cancer who relapsed after primary surgery performed between 2007 and 2016 were obtained from the SCANN study (Surveillance in Cervical CANcer). Factors related to the primary disease and recurrence were combined in a multivariable Cox proportional hazards model to predict PR-DSS. Results: The 5-year PR-DSS was 39.1% (95% confidence interval [CI] 22.7%-44.5%), median disease-free interval between primary surgery and recurrence (DFI1) was 1.5 years, and median survival after recurrence was 2.5 years. Six significant variables were identified in the multivariable analysis and were used to construct the prognostic model. Two were related to primary treatment (largest tumour size and lymphovascular space invasion) and four to recurrence (DFI1, age at recurrence, presence of symptoms, and recurrence type). The C-statistic after 10-fold cross-validation of prognostic model reached 0.701 (95% CI 0.675-0.727). Three risk-groups with significantly differing prognoses were identified, with 5-year PR-DSS rates of 81.8%, 44.6%, and 12.7%. Conclusions: We developed the robust model of PR-DSS to stratify patients with relapsed cervical cancer according to risk profiles

using six routinely recorded prognostic markers. The model can be utilised in clinical practice to aid decision-making on the strategy of recurrence management, and to better inform the patients.