1. **Quality and Performance of Papanicolaou Test using the Clinical and Laboratory Standards Institute (CLSI) EP12-A2 Guidelines: A Single-Center Study in Peru**
   Calidad y rendimiento de la prueba de Papanicolaou utilizando las pautas EP12-A2 del Clinical and Laboratory Standards Institute (CLSI): un estudio de un solo centro en Perú

INVESTIGADORES	:	Jeel Moya-Salazar, Jennifer Huarcaya, Diana Vazquéz, Víctor Rojas-Zumaran, Hans Contreras-Pulache.
REVISTA	:	J Cytol. 2023 Apr-Jun;40(2):81-87. doi: 10.4103/joc.joc_82_21. Epub 2023 May 22.
LINK	:	https://pubmed.ncbi.nlm.nih.gov/37388397/
TIPO DE CÁNCER	:	Ginecología
ABSTRACTO	:	Context: Quality assurance in cervical cytology is based on the cyto-histological correlation that is performed in several countries even without standardized protocols. Aims: To evaluate the quality of the Pap smear with the Clinical and Laboratory Standards Institute (CLSI) EP12-A2 guideline in a Peruvian hospital. Settings and design: This prospective study was carried out at tertiary care national hospital. Methods and material: The 156 cyto-histological results were collected and coded according to the Bethesda 2014 and FIGO system. The evaluation with the CLSI EP12-A2 guide allowed estimating the performance and quality of the test. Statistical analysis used: We performed a descriptive analysis of the cytological and histological data and correlation with the weight Kappa test. From the calculation of the likelihood ratios, the post-test probability was estimated using Bayes' theorem. Results: In cytology, 57 (36.5%) were undetermined abnormalities, 34 (21.8%) low-grade squamous intraepithelial lesion (SIL), and 42 (26.9%) high-grade SIL. Of the total biopsies, 56 (36.9%) were cervical intraepithelial neoplasia (CIN) grade 1, 23 (14.7%) were both CIN grade 2 and 3. We determined sensitivity, specificity, a positive and negative predictive value of 94%, 74.6%, 58%, and 97.1%, respectively. We determined a moderate cyto-histological agreement (κ = 0.57). Atypical squamous cells of undetermined significance (40%), and cannot exclude high-grade squamous intraepithelial lesions (42.1%) that showed higher overdiagnosis results. Conclusions: The quality and performance of the Papanicolaou test show high sensitivity and moderate specificity. The concordance found was moderate and the proportion of underdiagnosis was higher in abnormalities of undetermined significance.

2. **Survival associated with extent of radical hysterectomy in early-stage cervical cancer: a sub-analysis of the SCCAN collaborative study**
   Efecto de recibir un folleto personalizable sobre el conocimiento de los pacientes con cáncer de mama sobre su diagnóstico y tratamiento: un ensayo clínico aleatorizado

INVESTIGADORES	:	Nicolo Bizzarri, Denis Querleu, Lukas Dostalek, Luc R C W van Lonkhuijzen, Diana Giannarelli, Aldo Lopez, Sahar

Salehi, Ali Ayhan, Sarah H Kim, David Isla Ortiz, Jaroslav Klat, Fabio Landoni, Rene Pareja, Ranjit Manchanda, Jan Kosťun, Pedro T Ramirez, Mehmet M Meydanli, Diego Odetto, Rene Laky, Ignacio Zapardiel, Vit Weinberger, Ricardo Dos Reis, Luigi Pedone Anchora, Karina Amaro, Huseyin Akilli, Nadeem R Abu-Rustum, Rosa A Salcedo-Hernandez, Veronika Javurková, Constantijne H Mom, Giovanni Scambia, Henrik Falconer, David Cibula.

REVISTA : Am J Obstet Gynecol. 2023 Jun 17;S0002-9378(23)00422-2. doi: 10.1016/j.ajog.2023.06.030. Online ahead of print.

LINK : https://pubmed.ncbi.nlm.nih.gov/37336255/

TIPO DE CÁNCER : Ginecología

ABSTRACTO : Background: International guidelines recommend tailoring the radicality of hysterectomy according to the known pre-operative tumor characteristics in patients with early-stage cervical cancer. Objectives: The aim of this study was to assess whether increased radicality had an impact on 5-year disease-free survival (DFS) in patients with early-stage cervical cancer undergoing radical hysterectomy. Secondary aims were 5-year overall survival (OS) and pattern of recurrence. Study design: International, multicenter, retrospective study from the Surveillance in Cervical CANcer (SCCAN) collaborative cohort. Patients with FIGO 2009 stage IB1 and IIA1 who underwent open type B/C1/C2 radical hysterectomy according to Querleu-Morrow classification between January 2007 and December 2016, who did not undergo neo-adjuvant chemotherapy and who had negative lymph nodes and free surgical margins at final histology, were included. Descriptive statistics and survival analyses were performed. Patients were stratified according to pathologic tumor diameter. Propensity score match analysis was performed to balance baseline characteristics in patients undergoing nerve sparing and non-nerve sparing radical hysterectomy. Results: 1,257 patients were included. 883 (70.2%) underwent nerve sparing and 374 (29.8%) non-nerve sparing radical hysterectomy. Baseline differences between the study groups were found for tumor stage and diameter (higher use of non-nerve sparing radical hysterectomy for tumors >2 cm or with vaginal involvement; p<0.0001). The use of adjuvant therapy in patients undergoing nerve and non-nerve sparing radical hysterectomy was 27.3% versus 28.6%, respectively (p=0.63). 5-year DFS in patients undergoing nerve sparing versus non-nerve sparing radical hysterectomy was 90.1% (95%CI: 87.9-92.2) versus 93.8% (95%CI: 91.1-96.5), p=0.047, respectively. Non-nerve sparing radical hysterectomy was independently associated with better DFS at multivariable analysis performed on the entire cohort (HR:0.50, 95%CI:0.31-0.81; p=0.004). 5-year OS was: nerve-sparing 95.7% (95%CI: 94.1-97.2) versus non-nerve sparing 96.5%

(95%CI: 94.3-98.7), p=0.78. In patients with tumor diameter ≤20 mm 5-year DFS was 94.7% in nerve sparing versus 96.2% in non-nerve sparing (p=0.22). 5-year DFS was 90.3% in non-nerve sparing radical hysterectomy compared with 83.1% in nerve sparing radical hysterectomy (p=0.016) in patients with tumors between 21-40 mm (no significant difference in rate of adjuvant treatment in this subgroup, p=0.47). This was confirmed after propensity match score analysis (balancing the two study groups). Pattern of recurrence in the propensity matched population did not demonstrate any difference (p=0.70). Conclusion: For tumors ≤20 mm no survival difference was found with more radical hysterectomy. For tumors between 21-40 mm a more radical hysterectomy was associated with improved 5-year DFS. No difference in pattern of recurrence according to extent of radicality was observed. Non-nerve sparing radical hysterectomy was associated with better 5-year DFS compared with nerve-sparing radical hysterectomy after propensity score match analysis.

3. **Concurrence of primary extramammary Paget's disease of the vulva and vulval intra-epithelial neoplasia: A case report**
   Concurrencia de enfermedad de Paget primaria extramamaria de la vulva y neoplasia intraepitelial vulvar: reporte de un caso

INVESTIGADORES	Mercedes Bravo-Taxa, Luis Taxa-Rojas.
REVISTA	Case Reports Rev Esp Patol. 2023 Jul-Sep;56(3):196-200. doi: 10.1016/j.patol.2021.12.002. Epub 2022 Feb 15
LINK	https://pubmed.ncbi.nlm.nih.gov/37419559/
TIPO DE CÁNCER	Ginecología
ABSTRACTO	Extramammary Paget's disease and intraepithelial vulvar neoplasia are common lesions in the vulva. However, their simultaneous occurrence is extremely rare. We present the case of a 77year-old woman who presented with a 16month history of pruritus and a rash in the vulvar region with gradually increasing bleeding. She underwent a right hemivulvectomy and a left simple vulvectomy. The histopathology revealed a coexistence of both Paget's disease and high grade intraepithelial vulvar neoplasia.

4. **Uterine transposition and successful pregnancy in a patient with rectal cancer**
   Transposición uterina y embarazo exitoso en una paciente con cáncer de recto

INVESTIGADORES	Aldo Lopez, Joan Flaubert Perez Villena, Andres Guevara Jabiles, Karen Davila, Raymundo Sernaque Quintana, Reitan Ribeiro.
REVISTA	Int J Gynecol Cancer. 2023 Aug 7;33(8):1310-1315. doi: 10.1136/ijgc-2023-004661.
LINK	https://pubmed.ncbi.nlm.nih.gov/37549972/
TIPO DE CÁNCER	Ginecología

5. **MILACC study: could undetected lymph node micrometastases have impacted recurrence rate in the LACC trial?**
   Estudio MILACC: ¿podrían las micrometástasis no detectadas en los ganglios linfáticos haber impactado la tasa de recurrencia en el ensayo LACC?

INVESTIGADORES	Roni Nitecki, Pedro T Ramirez, Pavel Dundr, Kristyna Nemejcova, Reitan Ribeiro, Mariano Tamura Vieira Gomes, Ronaldo Luis Schmidt, Lucio Bedoya, David Ortiz Isla, Rene Pareja, Gabriel Jaime Rendón Pereira, Aldo Lopez, David Kushner, David Cibula.
REVISTA	Int J Gynecol Cancer. 2023 Aug 31;ijgc-2023-004711. doi: 10.1136/ijgc-2023-004711. Online ahead of print.
LINK	https://pubmed.ncbi.nlm.nih.gov/37652529/
TIPO DE CANCER	Ginecología
ABSTRACTO	Objective: The etiology of inferior oncologic outcomes associated with minimally invasive surgery for early-stage cervical cancer remains unknown. Manipulation of lymph nodes with previously unrecognized low-volume disease might explain this finding. We re-analyzed lymph nodes by pathologic ultrastaging in node-negative patients who recurred in the LACC (Laparoscopic Approach to Cervical Cancer) trial. Methods: Included patients were drawn from the LACC trial database, had negative lymph nodes on routine pathologic evaluation, and recurred to the abdomen and/or pelvis. Patients without recurrence or without available lymph node tissue were excluded. Paraffin tissue blocks and slides from all lymph nodes removed by lymphadenectomy were re-analyzed per standard ultrastaging protocol aimed at the detection of micrometastases (>0.2 mm and ≤2 mm) and isolated tumor cells (clusters up to 0.2 mm or <200 cells). Results: The study included 20 patients with median age of 42 (range 30-68) years. Most patients were randomized to minimally invasive surgery (90%), had squamous cell carcinoma (65%), FIGO 2009 stage 1B1 (95%), grade 2 (60%) disease, had no adjuvant treatment (75%), and had a single site of recurrence (55%), most commonly at the vaginal cuff (45%). Only one patient had pelvic sidewall recurrence in the absence of other disease sites. The median number of lymph nodes analyzed per patient was 18.5 (range 4-32) for a total of 412 lymph nodes. A total of 621 series and 1242 slides were reviewed centrally by the ultrastaging protocol. No metastatic disease of any size was found in any lymph node. Conclusions: There were no lymph node low-volume metastases among patients with initially negative lymph nodes who recurred in the LACC trial. Therefore, it is unlikely that manipulation of lymph nodes containing clinically undetected metastases is the underlying cause of the higher local recurrence risk in the minimally invasive arm of the LACC trial.

6. **First-Line Pembrolizumab + Chemotherapy Versus Placebo + Chemotherapy for Persistent, Recurrent, or Metastatic Cervical Cancer: Final Overall Survival Results of KEYNOTE-826**

   Pembrolizumab + quimioterapia de primera línea versus placebo + quimioterapia para el cáncer de cuello uterino persistente, recurrente o metastásico: resultados finales de supervivencia general de KEYNOTE-826

INVESTIGADORES Bradley J Monk, Nicoletta Colombo, Krishnansu S Tewari, Coraline Dubot, M Valeria Caceres, Kosei Hasegawa, Ronnie Shapira-Frommer, Pamela Salman, Eduardo Yañez, Mahmut Gümüş, Mivael Olivera Hurtado de Mendoza, Vanessa Samouëlian, Vincent Castonguay, Alexander Arkhipov, Cumhur Tekin, Kan Li, Stephen M Keefe, Domenica Lorusso; KEYNOTE-826 Investigators.

REVISTA J Clin Oncol. 2023 Nov 1:JCO2300914. doi: 10.1200/JCO.23.00914. Online ahead of print.

LINK https://pubmed.ncbi.nlm.nih.gov/37910822/

TIPO DE CÁNCER ginecología

ABSTRACTO Clinical trials frequently include multiple end points that mature at different times. The initial report, typically based on the primary end point, may be published when key planned co-primary or secondary analyses are not yet available. Clinical Trial Updates provide an opportunity to disseminate additional results from studies, published in JCO or elsewhere, for which the primary end point has already been reported.The phase III, double-blind KEYNOTE-826 trial of pembrolizumab 200 mg or placebo once every 3 weeks for up to 35 cycles plus platinum-based chemotherapy, with or without bevacizumab, showed statistically significant survival benefits with the addition of pembrolizumab for patients with persistent, recurrent, or metastatic cervical cancer (primary data cutoff: May 3, 2021). This article reports the protocol-specified final overall survival (OS) results tested in the PD-L1 combined positive score (CPS) ≥1, all-comer, and CPS ≥10 populations. At the final data cutoff (October 3, 2022), the median study follow-up duration was 39.1 months (range, 32.1-46.5 months). In the PD-L1 CPS ≥1 (N = 548), all-comer (N = 617), and CPS ≥10 (N = 317) populations, median OS with pembrolizumab-chemotherapy versus placebo-chemotherapy was 28.6 months versus 16.5 months (hazard ratio [HR] for death, 0.60 [95% CI, 0.49 to 0.74]), 26.4 months versus 16.8 months (HR, 0.63 [95% CI, 0.52 to 0.77]), and 29.6 months versus 17.4 months (HR, 0.58 [95% CI, 0.44 to 0.78]), respectively. The incidence of grade ≥3 adverse events was 82.4% with pembrolizumab-chemotherapy and 75.4% with placebo-chemotherapy. These results show that pembrolizumab plus chemotherapy, with or without bevacizumab, continued to provide clinically meaningful improvements in OS for patients with persistent, recurrent, or metastatic cervical cancer.

7. **Total uterine inversion due to pedunculated vaginal tumor**
   Inversión uterina total por tumor vaginal pediculado

INVESTIGADORES	Mario Humberto Castillo, Carlos Marrufo.
REVISTA	Int J Gynecol Cancer. 2023 Nov 20:ijgc-2023-004712. doi: 10.1136/ijgc-2023-004712. Online ahead of print.
LINCK	https://pubmed.ncbi.nlm.nih.gov/37989479/
TIPO DE CÁNCER	Ginecología
ABSTRACTO	Resumen no disponible

8. **Pembrolizumab or Placebo Plus Chemotherapy With or Without Bevacizumab for Persistent, Recurrent, or Metastatic Cervical Cancer: Subgroup Analyses from the KEYNOTE-826 Randomized Clinical Trial**
   Pembrolizumab o placebo más quimioterapia con o sin bevacizumab para el cáncer de cuello uterino persistente, recurrente o metastásico: análisis de subgrupos del ensayo clínico aleatorizado KEYNOTE-826

INVESTIGADORES	Krishnansu S Tewari, Nicoletta Colombo, Bradley J Monk, Coraline Dubot, M Valeria Cáceres, Kosei Hasegawa, Ronnie Shapira-Frommer, Pamela Salman, Eduardo Yañez, Mahmut Gümüs, Mivael Olivera Hurtado de Mendoza, Vanessa Samouëlian, Vincent Castonguay, Alexander Arkhipov, Cumhur Tekin, Kan Li, Sarper Toker, Stephen M Keefe, Domenica Lorusso.
REVISTA	JAMA Oncol. 2023 Dec 14:e235410. doi: 10.1001/jamaoncol.2023.5410. Online ahead of print.
LINK	https://pubmed.ncbi.nlm.nih.gov/38095881/
TIPO DE CÁNCER	Ginecología
ABSTRACTO	Importance: The KEYNOTE-826 randomized clinical trial showed statistically significant and clinically meaningful survival benefits with the addition of pembrolizumab to chemotherapy with or without bevacizumab in patients with persistent, recurrent, or metastatic cervical cancer. Treatment effects in patient subgroups of the study population are unknown. Objective: To assess efficacy outcomes in patient subgroups of KEYNOTE-826. Design, setting, and participants: Exploratory subgroup analyses were conducted in a global, phase 3, randomized, double-blind, placebo-controlled clinical trial. Participants included women with persistent, recurrent, or metastatic adenocarcinoma, adenosquamous carcinoma, or squamous cell carcinoma of the cervix that had not been treated with systemic chemotherapy and was not amenable to curative treatment. This subanalysis was conducted from November 20, 2018, to May 3, 2021. Interventions: Pembrolizumab, 200 mg, every 3 weeks or placebo for up to 35 cycles plus chemotherapy (paclitaxel, 175 mg/m2, plus cisplatin, 50 mg/m2, or carboplatin AUC 5 [area under the free carboplatin plasma concentration vs time curve]) with or without bevacizumab, 15 mg/kg. Main outcomes and measures: Overall survival (OS) and progression-free survival (PFS) by investigator assessment per Response Evaluation Criteria in Solid Tumors version 1.1 in subgroups defined by use

of bevacizumab (yes or no), choice of platinum (carboplatin or cisplatin), prior chemoradiotherapy (CRT) exposure only (yes or no), and histologic type (squamous or nonsquamous) in patients with programmed cell death ligand 1-positive tumors (defined as a combined positive score [CPS] ≥1) and in the intention-to-treat population. Results: A total of 617 patients (median age, 51 years; range, 22-82 years) were enrolled in the trial. In the CPS greater than or equal to 1 population, hazard ratios (HRs) for OS favored the pembrolizumab group in all subgroups: with bevacizumab (HR, 0.62; 95% CI, 0.45-0.87) and without bevacizumab (HR, 0.67; 95% CI, 0.47-0.96), use of carboplatin (HR, 0.65; 95% CI, 0.50-0.85) and cisplatin (HR, 0.53; 95% CI, 0.27-1.04), with prior CRT only (HR, 0.56; 95% CI, 0.39-0.81) and without prior CRT only (HR, 0.72; 95% CI, 0.52-1.00), and squamous (HR, 0.60; 95% CI, 0.46-0.79) and nonsquamous (HR, 0.70; 95% CI, 0.41-1.20) histologic type. In the intention-to-treat population, HRs for OS also favored the pembrolizumab group in all subgroups: with bevacizumab (HR, 0.63; 95% CI, 0.47-0.87) and without bevacizumab (HR, 0.74; 95% CI, 0.53-1.04), use of carboplatin (HR, 0.69; 95% CI, 0.54-0.89) or cisplatin (HR, 0.59; 95% CI, 0.32-1.09), with prior CRT only (HR, 0.64; 95% CI, 0.45-0.91) and without prior CRT only (HR, 0.71; 95% CI, 0.53-0.97), and squamous (HR, 0.61; 95% CI, 0.47-0.80) and nonsquamous (HR, 0.76; 95% CI, 0.47-1.23) histologic type. Similar to OS, the addition of pembrolizumab prolonged PFS across all subgroups in the CPS greater than or equal to 1 and intention-to-treat populations. Conclusions and relevance: The findings of this trial suggest that adding pembrolizumab to chemotherapy with or without bevacizumab improved OS across subgroups of patients with persistent, recurrent, or metastatic cervical cancer.

9. **Durvalumab versus placebo with chemoradiotherapy for locally advanced cervical cancer (CALLA): a randomised, double-blind, phase 3 trial**

Durvalumab versus placebo con quimiorradioterapia para el cáncer de cuello uterino localmente avanzado (CALLA): un ensayo de fase 3 aleatorizado, doble ciego

INVESTIGADORES	Bradley J Monk, Takafumi Toita, Xiaohua Wu, Juan C Vázquez Limón, Rafal Tarnawski, Masaki Mandai, Ronnie Shapira-Frommer, Umesh Mahantshetty, Maria Del Pilar Estevez-Diz, Qi Zhou, Sewanti Limaye, Francisco J Ramirez Godinez, Christina Oppermann Kussler, Szilvia Varga, Natalia Valdiviezo, Daisuke Aoki, Manuel Leiva, Jung-Yun Lee, Raymond Sulay, Yulia Kreynina, Wen-Fang Cheng, Felipe Rey, Yi Rong, Guihao Ke, Sophie Wildsmith, Andrew Lloyd, Hannah Dry, Ana Tablante Nunes, Jyoti Mayadev.
REVISTA	Clinical Trial Lancet Oncol. 2023 Dec;24(12):1334-1348. doi: 10.1016/S1470-2045(23)00479-5.
LINK	https://pubmed.ncbi.nlm.nih.gov/38039991/
TIPO DE CÁNCER	Ginecología
ABSTRACTO	Background: Concurrent chemoradiotherapy has been the standard of care for locally advanced cervical cancer for over 20

years; however, 30-40% of treated patients have recurrence or progression within 5 years. Immune checkpoint inhibition has improved outcomes for patients with PD-L1 positive metastatic or recurrent cervical cancer. We assessed the benefit of adding durvalumab, a PD-L1 antibody, with and following chemoradiotherapy for locally advanced cervical cancer. Methods: The CALLA randomised, double-blind, phase 3 trial included 105 hospitals across 15 countries. Patients aged at least 18 years with previously untreated locally advanced cervical cancer (adenocarcinoma, squamous, or adenosquamous; International Federation of Gynaecology and Obstetrics [FIGO] 2009 stage IB2-IIB lymph node positive, stage ≥III any lymph node status) and WHO or Eastern Cooperative Oncology Group performance status of 0 or 1 were randomly assigned (1:1) through an interactive web response system using a permuted block size of 4 to receive durvalumab (1500 mg intravenously once every 4 weeks) or placebo with and following chemoradiotherapy, for up to 24 cycles. Chemoradiotherapy included 45 Gy external beam radiotherapy at 5 fractions per week concurrent with intravenous cisplatin (40 mg/m2) or carboplatin (area under the concentration-time curve 2) once weekly for 5 weeks, followed by image-guided brachytherapy (high-dose rate, 27·5-30 Gy or low-dose/pulse-dose rate, 35-40 Gy). Randomisation was stratified by disease stage status (FIGO stage and node status) and geographical region. Chemoradiotherapy quality was continuously reviewed. The primary endpoint was progression-free survival, assessed by the investigator using Response Evaluation Criteria in Solid Tumors, version 1.1, in the intention-to-treat population. Safety was assessed in patients who received at least one dose of study treatment. This study is registered with ClinicalTrials.gov, NCT03830866. Findings: Between Feb 15, 2019, and Dec 10, 2020, 770 women were randomly assigned (385 to durvalumab and 385 to placebo; median age 49 years [IQR 41-57]). Median follow-up was 18·5 months (IQR 13·2-21·5) in the durvalumab group and 18·4 months (13·2-23·7) in the placebo group. At data cutoff, median progression-free survival had not been reached (95% CI not reached-not reached) for either group (HR 0·84; 95% CI 0·65-1·08; p=0·17); 12-month progression-free survival was 76·0% (71·3-80·0) with durvalumab and 73·3% (68·4-77·5) with placebo. The most frequently reported grade 3-4 adverse events in both groups were anaemia (76 [20%] of 385 in the durvalumab group vs 56 [15%] of 384 in the placebo group) and decreased white blood cells (39 [10%] vs 49 [13%]). Serious adverse events occurred for 106 (28%) patients who received durvalumab and 89 (23%) patients who received placebo. There were five treatment-related deaths in the durvalumab group (one case each of urinary tract infection, blood loss anaemia, and pulmonary embolism related to chemoradiotherapy only; one case of endocrine disorder related to durvalumab only; and one case of sepsis related to both durvalumab and chemoradiotherapy). There was one treatment-related death in

the placebo group (pneumonia related to chemoradiotherapy). Interpretation: Durvalumab concurrent with chemoradiotherapy was well tolerated in participants with locally advanced cervical cancer, however it did not significantly improve progression-free survival in a biomarker unselected, all-comers population. Concurrent durvalumab plus chemoradiotherapy warrants further exploration in patients with high tumoral PD-L1 expression. Rigorous monitoring ensured high chemoradiotherapy compliance with advanced technology and allowed patients to receive optimal care.