1. **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.
   LINK: https://pubmed.ncbi.nlm.nih.gov/38095881/
   REVISTA: Clinical Trial JAMA Oncol. 2024 Feb 1;10(2):185-192. doi: 10.1001/jamaoncol.2023.5410
   ASTRACTO: 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.

2. **LACC Trial: Final Analysis on Overall Survival Comparing Open Versus Minimally Invasive Radical Hysterectomy for Early-Stage Cervical Cancer**
   Ensayo LACC: Análisis final sobre la supervivencia general que compara la histerectomía radical abierta versus la mínimamente invasiva para el cáncer de cuello uterino en etapa temprana

   INVESTIGADORES: Pedro T Ramirez, Kristy P Robledo, Michael Frumovitz, Rene Pareja, Reitan Ribeiro, Aldo Lopez, Xiaojian Yan, David Isla, Renato Moretti, Marcus Q Bernardini, Val Gebski, Rebecca Asher, Vanessa Behan, Robert L Coleman, Andreas Obermai.
   LINK: https://pubmed.ncbi.nlm.nih.gov/38810208/
   REVISTA: J Clin Oncol. 2024 May 29:JCO2302335. doi: 10.1200/JCO.23.02335. Online ahead of print.
   ASTRACTO: 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 aim of this study was to compare overall survival between open and minimally invasive radical hysterectomy with participants followed for 4.5 years. The primary objective was to evaluate whether minimally invasive surgery was noninferior in disease-free survival (DFS) to abdominal radical hysterectomy. Secondary outcomes included overall survival. Sample size was based on DFS of 90% at 4.5 years and 7.2% noninferiority margin for minimally invasive surgery. A total of 631 patients were enrolled: 319 assigned to minimally invasive and 312 to open surgery. Of these, 289 (90.6%) patients underwent minimally invasive surgery and 274 (87.8%) patients open surgery. At 4.5 years, DFS was 85.0% in the minimally invasive group and 96% in the open group (difference of -11.1; 95% CI, -15.8 to -6.3; P = .95 for noninferiority). Minimally invasive surgery was associated with lower rate of DFS compared with open surgery (hazard ratio [HR], 3.91 [95% CI, 2.02 to 7.58]; P < .001). Rate of overall survival at 4.5 years was 90.6% versus 96.2% for the minimally invasive and open surgery groups, respectively (HR for death of any cause = 2.71 [95% CI, 1.32 to 5.59]; P = .007). Given higher recurrence rate and worse overall survival with minimally invasive surgery, an open approach should be standard of care.

1. **Total uterine inversion due to pedunculated vaginal tumor**
   Inversión uterina total debido a tumor vaginal pediculado

   INVESTIGADORES: Mario Humberto Castillo, Carlos Marrufo
   LINK: https://pubmed.ncbi.nlm.nih.gov/37989479/
   REVISTA: Case Reports Int J Gynecol Cancer. 2024 Feb 5;34(2):349-350. doi: 10.1136/ijgc-2023-004712.

2. **Survival associated with the use of sentinel lymph node in addition to lymphadenectomy in early-stage cervical cancer treated with surgery alone: A sub-analysis of the Surveillance in Cervical CANcer (SCCAN) collaborative study**
   Supervivencia asociada al uso del ganglio linfático centinela además de la linfadenectomía en el cáncer de cuello uterino en etapa temprana tratado solo con cirugía: un subanálisis del estudio colaborativo Surveillance in Cervical CANcer (SCCAN)

   INVESTIGADORES: Nicolò Bizzarri, Denis Querleu, Pedro T Ramirez, Lukáš Dostálek, Luc Rc 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, 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-Hernández, Veronika Javůrková, Constantijne H Mom, Henrik Falconer, Giovanni Scambia, David Cibula.
   LINK: https://pubmed.ncbi.nlm.nih.gov/39270379/
   REVISTAS: Multicenter Study Eur J Cancer. 2024 Nov:211:114310. doi: 10.1016/j.ejca.2024.114310. Epub 2024 Sep 12.
   ABSTRACTO: Aim: The aim of this study was to assess whether the use of sentinel lymph node (SLN) in addition to lymphadenectomy was associated with survival benefit in patients with early-stage cervical cancer. Methods: International, multicenter, retrospective study. Inclusion criteria: cervical cancer treated between 01/2007 and 12/2016 by surgery only; squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma, FIGO 2009 stage IB1-IIA2, negative surgical margins, and laparotomy approach. Patients undergoing neo-adjuvant and/or adjuvant treatment and/or with positive para-aortic lymph nodes, were excluded. Women with positive pelvic nodes who refused adjuvant treatment, were included. Lymph node assessment was performed by SLN (with ultrastaging protocol) plus pelvic lymphadenectomy ('SLN' group) or pelvic lymphadenectomy alone ('non-SLN' group). Results: 1083 patients were included: 300 (27.7 %) in SLN and 783 (72.3 %) in non-SLN group. 77 (7.1 %) patients had recurrence (N = 11, 3.7 % SLN versus N = 66, 8.4 % non-SLN, p = 0.005) and 34 (3.1 %) (N = 4, 1.3 % SLN versus N = 30, 3.8 % non-SLN, p = 0.033) died. SLN group had better 5-year disease-free survival (DFS) (96.0 %,95 %CI:93.5-98.5 versus 92.0 %,95 %CI:90.0-94.0; p = 0.024). No 5-year overall survival (OS) difference was shown (98.4 %,95 %CI:96.8-99.9 versus 96.8 %,95 %CI:95.4-98.2; p = 0.160). SLN biopsy and lower stage were independent factors associated with improved DFS (HR:0.505,95 %CI:0.266-0.959, p = 0.037 and HR:2.703,95 %CI:1.389-5.261, p = 0.003, respectively). Incidence of pelvic central recurrences was higher in the non-SLN group (1.7 % versus 4.5 %, p = 0.039). Conclusion: Adding SLN biopsy to pelvic lymphadenectomy was associated with lower recurrence and death rate and improved 5-year DFS. This might be explained by the

lower rate of missed nodal metastasis thanks to the use of SLN ultrastaging. SLN biopsy should be recommended in patients with early-stage cervical cancer.

3. **The prognosis of stage IA cervical cancer: Subgroup analysis of the SCCAN study**
   Pronóstico del cáncer de cuello uterino en estadio IA: análisis de subgrupos del estudio SCCAN

   INVESTIGADORES: Zheng Yuan Ng, Ranjit Manchanda, Aldo Lopez, Andreas Obermair, Lukas Dostalek, Rene Pareja, Luc R C W van Lonkhuijzen, Henrik Falconer, David Isla Ortiz, Anna Fagotti, Pedro T Ramirez, Fabio Landoni, Vit Weinberger, Rene Laky, Sarah H Kim, Jaroslav Klat, Roman Kocian, Darwin Pari, Martina Borcinova, Kristyna Nemejcova, David Cibula.
   LINK: https://pubmed.ncbi.nlm.nih.gov/39378742/
   REVISTAS: Gynecol Oncol. 2024 Oct 7:191:95-99. doi: 10.1016/j.ygyno.2024.09.022. Online ahead of print.
   ABSTRACTO: Objective: Patients with TNM T1a cervical cancer have excellent prognosis; however, the risk for recurrence remains an issue of concern and management guidelines are based on limited data. Here we performed subgroup analysis of the Surveillance in Cervical Cancer (SCCAN) consortium with the objective of defining the prognosis of T1a cervical cancer patients. Methods: SCCAN was an international, multicentric, retrospective cohort study of patients with cervical cancer undergoing surgical treatment in tertiary centers. Inclusion criteria included: histologically confirmed cervical cancer treated between 2007 and 2016; TNM T1a; primary surgical management; and at least 1-year of follow-up data availability. Exclusion criteria included treatment with primary chemo-radiation, and missing treatment-related or clinical data. Results: Out of 975 patients included, 554 (57 %) were T1a1 and 421 (43 %) T1a2. The majority had squamous-cell carcinoma (78 %). 79 patients (8.1 %) had lymphovascular space invasion (LVSI). 455 patients (47 %) underwent radical hysterectomy/ parametrectomy. Laparoscopic and open surgery was performed in 401 (41 %) and in 361 (37 %) patients, respectively. Adjuvant treatment was administered to 56 patients (5.7 %). Assessment of lymph nodes (LN) was performed in 524 patients (54 %), with LN involvement found in 15 (2.9 %). There were 40 (4.1 %) recurrences, occurring at a median of 26 months (4-106), out of which 33 (82.5 %) occurred in pelvis. Among T1a1 cases, there were 10 recurrences (2.0 %) if LVSI was negative, and 3 recurrences (6.7 %) if LVSI was positive. Among T1a2 cases, there were 23 recurrences (6.7 %) if LVSI was negative, and 4 recurrences (5.1 %) if LVSI was positive. There were 3 recurrences in the LN+ group (recurrence rate 20 %). Conclusions: The risk of recurrence in T1a cervical cancer was 4.1 % corresponding to the rates seen in patients with FIGO 1B cancer in recently published prospective trials. LN involvement represents a risk factor for disease recurrence. Our results indicate that stage T1a cervical cancer, apart from T1a1 LVSI negative disease, should follow the same principles in the management as that of FIGO stage 1B cancer.

4. **Pembrolizumab Plus Chemotherapy for Advanced and Recurrent Cervical Cancer: Final Analysis According to Bevacizumab Use in the Randomized KEYNOTE-826 Study**
   Pembrolizumab más quimioterapia para el cáncer de cuello uterino avanzado y recurrente: análisis final según el uso de bevacizumab en el estudio aleatorizado KEYNOTE-826

   INVESTIGADORES: D Lorusso, N Colombo, C Dubot, M V Cáceres, K Hasegawa, R Shapira-Frommer, P Salman, E Yañez, M Gümüş, M Olivera, V Samouëlian, V Castonguay, A Arkhipov, K Li, S Toker, C Tekin, K S Tewari, B J Monk.
   LINK: https://pubmed.ncbi.nlm.nih.gov/39393777/
   REVISTA: Ann Oncol. 2024 Oct 9:S0923-7534(24)04033-X. doi: 10.1016/j.annonc.2024.10.002. Online ahead of print.
   ABSTRACTO: Background: In KEYNOTE-826 (NCT03635567), pembrolizumab plus chemotherapy (± bevacizumab) significantly improved overall survival (OS) and progression-free survival (PFS) in patients with persistent, recurrent, or metastatic cervical cancer. This exploratory analysis examined outcomes in patient subgroups defined by bevacizumab use. Patients and methods: Eligible adult patients had persistent, recurrent, or metastatic squamous cell carcinoma, adenosquamous carcinoma, or adenocarcinoma of the cervix not previously treated with chemotherapy and not amenable to curative treatment; measurable disease per RECIST v1.1; and an Eastern Cooperative Oncology Group performance status ≤1. Patients were randomized 1:1 to pembrolizumab 200 mg every 3 weeks or placebo for up to 35 cycles plus chemotherapy (± bevacizumab 15 mg/kg). Dual primary endpoints were OS and PFS per RECIST v1.1 by investigator assessment. Outcomes were assessed in subgroups defined by bevacizumab use. Hazard ratios (HRs) and 95% CIs were based on a stratified Cox regression model. Results: 617 patients were randomized (pembrolizumab arm, n=308 [63.6% with bevacizumab]; placebo arm, n=309 [62.5% with bevacizumab]). The most common reason for bevacizumab exclusion was medical contraindication (75.9%). Among patients who received bevacizumab, HRs (95% CIs) for PFS favored the pembrolizumab arm in the PD-L1 combined positive score (CPS) ≥1 (0.56 [0.43-0.73]) and all-comer (0.57 [0.45-0.73]) populations; OS results were 0.60 (0.45-0.79) and 0.61 (0.47-0.80), respectively. Among patients who did not receive bevacizumab, HRs (95% CIs) for PFS also favored the pembrolizumab arm in the PD-L1 CPS≥1 (0.61 [0.44-0.85]) and all-comer (0.69 [0.50-0.94]) populations; OS results were 0.61 (0.44-0.85) and 0.67 (0.49-0.91), respectively. Among patients who received bevacizumab, grade ≥3 treatment-related adverse events occurred in 74.0% of patients in the pembrolizumab arm and 66.8% in the placebo arm. Conclusion: Pembrolizumab plus chemotherapy prolonged PFS and OS and had manageable safety compared with placebo plus chemotherapy in patient subgroups defined by bevacizumab use.