An International Randomized Phase III Trial Comparing Radical Hysterectomy and Pelvic Node Dissection (RH) vs Simple Hysterectomy and Pelvic Node Dissection (SH) in Patients with Low-Risk Early-Stage Cervical Cancer (LRESCC). A Gynecologic Cancer Intergroup Study led by Canadian Cancer Trials Group (CCTG CX.5-SHAPE).

Background:
Retrospective data suggests that less radical surgery may be safe and associated with less morbidity. The objective of this non-inferiority phase III trial was to compare RH to SH in women with LRESCC.

Methods:
Women with LRESCC defined as stage IA2 or IB1 disease with lesions ≤2cm were randomized to RH or SH. The primary endpoint was pelvic recurrence rate at 3 years (PRR3). Primary intention to treat (ITT) analysis included all patients randomized. Secondary endpoints included extra-pelvic relapse-free survival (EPRFS) and overall survival (OS).

Results:
700 women were enrolled from December 2012 to November 2019. Patient characteristics were well balanced: median age 44 (24-80); 91.7% were stage 1B1 and 61.7% were squamous histology. On final pathology, lymph node metastasis occurred in 3.7% (3.3% SH and 4.4% RH), positive margins in 2.5% (2.1% SH and 2.9% RH), and lesions >2cm in 4.25% (4.4% SH and 4.1% RH). A total of 8.8% of women received post-surgical adjuvant therapy (9.2% SH and 8.4% RH). With a median follow-up of 4.5 years, 21 pelvic recurrences occurred (11 SH and 10 RH). The PRR3 was 2.52% with SH and 2.17% with RH (difference 0.35% with 95% upper confidence limit 2.32%) in ITT analysis. The 3-year EPRFS and OS were respectively 98.1% and 99.1% with SH; 99.7% and 99.4% with RH. SH had less bladder (9 vs 3) and ureteral injuries (5 vs 3) and significantly less urinary incontinence (4.7% vs. 11.0%; $p=0.003$) and urinary retention (0.6% vs. 9.9%; $p<0.0001$) compared to RH. On multivariate analysis, there was no significant difference in pelvic or extra-pelvic recurrences following SH or RH according to surgical approach (abdominal vs MIS).

Conclusion:
The PRR3 in women with LRESCC who underwent SH was not inferior to RH and associated with fewer surgical complications. SH should be considered the new standard of care.