

Question 17 (Systematic Review)

For women who have been treated for adenocarcinoma in situ (AIS) with cone excision or LEEP and with clear histologic margins what is the safety and effectiveness of cytology and HPV testing at 12 and 24 months and discharging if double-negative at both visits vs completion hysterectomy or annual cytology?

Search terms: Adenocarcinoma in situ, AIS, cervical adenocarcinoma, recurrent, test of cure, treatment, surveillance, post-treatment, follow-up, human papillomavirus, HPV, papillomavirus infections. Search was conducted from 2004-current with articles limited to the English language.

Results: No papers were found that would directly address the question, however the following study may provide some useful information.

Author	Country	Study Type	Subjects	Findings
Costa et al, 2007	Italy	Case series	<p>42 consecutive women (mean age 40.5y; range 27–63 years) diagnosed with AIS on conization (cold knife, LEEP or laser) and followed up for a mean of 40 months using colposcopy, PAP smear, endocervical curettage and HPV (Hybrid Capture II) testing repeated at 6-month intervals.</p> <p>51.2% margins clear 4/42 had SCC on initial cone biopsy</p> <p>5/42 underwent subsequent hysterectomy for reasons other than persistent positive margins 13/42 underwent subsequent hysterectomy for persistent positive margins</p>	<p>Persistent or recurrent disease was observed in 17 (40.4%) cases – 5 diagnosed on subsequent conisation including 1 adenocarcinoma 12 diagnosed on hysterectomy including 4 adenocarcinomas and 1 SCC</p> <p>With mean follow up of 40 months Of 20 women with involved margins at baseline 55% (11/20) were diagnosed subsequently with residual disease. Of 21 women with free margins at baseline 28.6% (6/21) were diagnosed subsequently with residual disease.</p> <p>Of 13 women who underwent hysterectomy for persistent positive margins 12/13 (92%) had residual disease Of 5 women who underwent hysterectomy for reasons other than persistent positive margins none were found to have residual disease</p> <p>Using colposcopy and biopsy (less than perfect) as gold standard</p> <p>At the 1st follow-up</p>

				<ul style="list-style-type: none"> • Pap smear had 60% sensitivity and NPV of 73.3% • Co-testing had a sensitivity of 90%, and NPV of 88.9%. <p>At the 2nd follow-up</p> <ul style="list-style-type: none"> • Pap smear had 66.7% sensitivity and NPV of 87.5% • Co-testing had a sensitivity of 100%, and NPV of 100%. <p>At the 3rd follow-up - virtually no disease detected</p> <ul style="list-style-type: none"> • Pap smear had 0% sensitivity and NPV of 91.3% • Co-testing had a sensitivity of 0%, and NPV of 91.7%. <p>No disease detected at 4th, 5th or 6th follow-ups</p>
Costa et al, 2012	Italy	Prospective	119 women diagnosed with AIS on conization (cold knife, LEEP, laser or needle) and managed conservatively with follow-up for a mean of 41 months using colposcopy, PAP smear and endocervical and exocervical brush cytology repeated at 6-month intervals for 3 years followed by annual follow-up. 95 women were followed up with HPV (Hybrid Capture II) testing. 51.8% margins clear	<p>Hr-HPV detection on follow-up significantly increased risk of recurrent and progressive disease</p> <p>Abnormal Pap smear on follow-up significantly increased risk of persistent disease</p> <p>Having involved margins significantly increased risk of progressive disease</p>

NPV = negative predictive value; SCC = squamous cell carcinoma

References

- Costa S, Negri G, Sideri M, Santini D, Martinelli G, Venturoli S, et al. **Human papillomavirus (HPV) test and PAP smear as predictors of outcome in conservatively treated adenocarcinoma in situ (AIS) of the uterine cervix.** Gynecol Oncol 2007 Jul;106(1):170-6
- Costa S, Venturoli S, Negri G, Sideri M, Santini D, Petri M, Pesaresi M, et al. Factors predicting the outcome of conservatively treated adenocarcinoma **in situ of the uterine cervix: An analysis of 166 cases.** Gynecol Oncol 2012;124:490-495