ATHENA Trial CIN 2+ Cervical Biopsy Misclassifications Raise Questions

To the Editor

We read with interest the report by Stoler et al1 documenting pathologic misclassification of cervical intraepithelial neoplasia (CIN) 2+ cases in the ATHENA (Addressing THE Need for Advanced Diagnostics) trial. Of the 8 cervical biopsy specimens that were diagnosed as CIN 2 or worse (CIN 2+) but that were high-risk human papillomavirus (HPV)-negative by the cobas HPV test (Roche Molecular Systems, Pleasanton, CA), at least 5 (63%) of 8 CIN 2+ diagnoses were not confirmed when p16 immunohistochemical analyses were performed.1

Previous studies have documented that p16 is a useful and reliable diagnostic adjunct for distinguishing biopsy specimens with and without CIN 2+.2,3 Because the authors document misclassification of CIN 2+ diagnoses in women younger than 40 years and older than 40 years and because the trial was based on routine H&E-stained slides without p16 evaluations for diagnosis, it is not unreasonable to wonder how many other ATHENA CIN 2+ diagnoses may actually represent pathologic misclassifications. Histopathologic misclassification of CIN 2+ could also help partially explain the puzzlingly low sensitivity (35.9%) of liquid-based cytology for CIN 2+ detection in the study.4 In contrast, for example, another large HPV trial recently reported liquid-based cytology sensitivity for CIN 3+ detection at 89.0%.5

Robert Marshall Austin, MD, PhD
Pathology Department
Magee-Womens Hospital of University of Pittsburgh Medical Center
Pittsburgh, PA

References