Put It on the Board

Recommendations released for use of dual stain to triage HPV-positive results

April 2024—Member organizations of the Enduring Consensus Cervical Cancer Screening and Management Guidelines effort released in March their recommendations for the use of p16/Ki-67 dual stain for managing individuals who test positive for HPV.

Dual staining of cytology specimens detects a marker of HPV-related oncogene activity (p16) and a marker of cell proliferation (Ki-67), which, when detected together in the same cell, is indicative of cell cycle dysregulation associated with transforming HPV infections and strongly associated with precancerous cellular changes (CIN3+). Roche's CINtec Plus Cytology is the only FDA-approved dual stain triage test for HPV-positive cervical cancer screening results.

To ensure the applicability of the dual stain recommendations to different populations, the group reports that they assessed risk estimates in two distinct cohorts. One is the Kaiser Permanente Northern California cohort, which was the main data set used for the 2019 American Society for Colposcopy and Cervical Pathology consensus guidelines for managing abnormal cervical cancer screening tests and cancer precursors. The other data set comes from the Studying Risk to Improve Disparities, or STRIDES, study in Mississippi.

For triage of positive HPV results from screening with primary HPV testing (with or without genotyping) or with cytology cotesting, colposcopy is recommended for those who test dual stain positive. For those who test dual stain negative, one-year follow-up with HPV-based testing is recommended (except for HPV16- and HPV18-positive results, or high-grade cytology in cotesting, for which the recommendation is immediate colposcopy referral).

The Enduring Guidelines process is an effort to keep cervical cancer screening and management guidelines up to date. Among its many organizational members are the National Cancer Institute, the ASCCP and CAP, and the Papanicolaou Society of Cytopathology.

The full set of recommendations is at https://shorturl.at/hktzF.

CAP updates principles of analytic validation of IHC assays

A CAP expert panel performed a review of the literature and updated the 2014 guideline that provided recommendations for analytic validation of clinical immunohistochemistry assays. The guideline update, released in February, consists of two strong recommendations, one conditional recommendation, and 12 good practice statements (Goldsmith JD, et al. *Arch Pathol Lab Med*. Published online Feb. 23, 2024. doi:10.5858/arpa.2023-0483-CP).

Many of the original guideline statements remain similar, the authors write, but new recommendations address analytic validation of assays with distinct scoring systems, such as programmed death receptor-1 and analytic verification of FDA-approved or -cleared assays. More specific guidance is provided on validating IHC performed on cytology specimens.

The two strong recommendations are as follows:

- For initial analytic validation or verification of every assay used clinically, laboratories should achieve at least 90 percent overall concordance between the new assay and the comparator assay or expected results.
- For initial analytic validation of lab-developed assays and verification of

FDA-approved or -cleared predictive IHC assays with distinct scoring schemes (e.g. HER2, PD-L1), labs should separately validate or verify each assay-scoring system combination with a minimum of 20 positive and 20 negative tissues. The set should include challenges based on the intended clinical use of the assay.

For cytologic specimens, a conditional recommendation and good practice statement, respectively, follow:

- For analytic validation of IHC performed on cytologic specimens that are not fixed in the same manner as the tissues used for initial assay validation, labs should perform separate validations for every new analyte and corresponding fixation method before placing them into clinical service.
- A minimum of 10 positive and 10 negative cases is recommended for each validation performed on cytologic specimens, if possible. The lab medical director should consider increasing the number of cases if predictive markers are being validated. If the minimum of 10 positive and 10 negative cases is not feasible, the rationale for using fewer cases should be documented.

The full guideline update is at https://bit.ly/CAP-IHCassay.

Labcorp to acquire select assets of BioReference Health

Labcorp has entered into an agreement to acquire select assets of BioReference Health, a wholly owned subsidiary of Opko Health.

Through this transaction, Labcorp will acquire BioReference Health's laboratory testing businesses focused on clinical diagnostics and reproductive and women's health across the United States outside of New York and New Jersey. The transaction includes patient service centers and certain customer contracts and operating assets. BioReference Health will continue to offer oncology and urology diagnostic services nationwide and maintain its full operations in New York and New Jersey.

The assets Labcorp will acquire currently generate about $100 million in annual revenue. The purchase price for the transaction is $237.5 million. The transaction is expected to close in the second half of this year.