COLLEGE of AMERICAN PATHOLOGISTS

ASCO GUIDELINES

Summary of ASCO/CAP ER and PgR Guideline Recommendations

Optimal algorithm for ER/PgR testing

Recommendation:

Positive for ER or PgR if finding of ≥ 1% of tumor cell nuclei are immunoreactive.

Negative for ER or PgR if finding of < 1% of tumor cell nuclei are immunoreactive in the presence of evidence that the sample can express ER or PgR (positive intrinsic controls are seen).

Uninterpretable for ER or PgR if finding that no tumor nuclei are immunoreactive and that internal epithelial elements present in the sample or separately submitted from the same sample lack any nuclear staining.

Comments:

These definitions depend on laboratory documentation of the following:

1. Proof of initial validation in which positive ER or PgR categories are 90% concordant and negative ER or PgR categories are 95% concordant with a clinically validated ER or PgR assay.
2. Ongoing internal QA procedures, including use of external controls of variable ER and PgR activity with each run of assay, regular assay reassessment, and competency assessment of technicians and pathologists.
3. Participation in external proficiency testing according to the proficiency testing program guidelines.
4. Biennial accreditation by valid accrediting agency.

Optimal testing conditions

Recommendation:

Large, preferably multiple core biopsies of tumor are preferred for testing if they are representative of the tumor (grade and type) at resection.

Comments:

Specimen should be rejected and testing repeated on a separate sample if any of the following conditions exist:

1. External controls are not as expected (scores recorded daily show variation).
2. Artifacts involve most of sample.

Specimen may also be rejected and testing repeated on another sample if:

1. Slide has no staining of included normal epithelial elements and/or normal positive control on same slide.
2. Specimen has been decalcified using strong acids.
3. Specimen shows an ER-negative/PgR-positive phenotype (to rule out a false-negative ER assay or a false-positive PgR assay).
4. Sample has prolonged cold ischemia time or fixation duration, < 6 hours or > 72 hours and is negative on testing in the absence of internal control elements.

Recommendation:

Interpretation follows guideline recommendation.

Comments:

Positive ER or PgR requires that ≥ 1% of tumor cells are immunoreactive. Both average intensity and extent of staining are reported. Image analysis is a desirable method of quantifying percentage of tumor cells that are immunoreactive.

H score, Allred score, or Quick score may be provided.

Negative ER or PgR requires < 1% of tumor cells with ER or PgR staining. Interpreters have method to maintain consistency and competency documented regularly.

Accession slip and report must include guideline-detailed elements.

Recommendation:

Accession slip and report must include guideline-detailed elements.

Hammond MEH, Hayes DF, Dowsett M, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. *Arch Pathol Lab Med*. 2010;134:907–922.

Summary of ASCO/CAP ER and PgR Guideline Recommendations

Optimal tissue handling requirements*
***Revised per the 2011 ASCO/CAP Clinical Notice on HER2 and ER/PgR**

Recommendation:

Time from tissue acquisition to fixation should be ≤ one hour. Samples for ER and PgR testing are fixed in 10% NBF for 6–72 hours. Samples should be sliced at 5-mm intervals after appropriate gross inspection and margins designation and placed in sufficient volume of NBF to allow adequate tissue penetration. If tumor comes from remote location, it should be bisected through the tumor on removal and sent to the laboratory immersed in a sufficient volume of NBF. Cold ischemia time, fixative type, and time the sample was placed in NBF must be recorded.

As in the ASCO/CAP HER2 guideline, storage of slides for more than 6 weeks before analysis is not recommended.

Time tissue is removed from patient, time tissue is placed in fixative, duration of fixation, and fixative type must be recorded and noted on accession slip or in report.

Optimal internal validation procedure

Recommendation:

Validation of any test must be done before test is offered. See separate article on testing validation (Fitzgibbons et al[1]).

Validation must be done using a clinically validated ER or PgR test method.

Revalidation should be done whenever there is a significant change to the test system, such as a change in the primary antibody clone or introduction of new antigen retrieval or detection systems.

Optimal internal QA procedures

Recommendation:

Initial test validation. See separate article on testing validation (Fitzgibbons et al[1]).

Ongoing quality control and equipment maintenance.

Initial and ongoing laboratory personnel training and competency assessment.

Use of standardized operating procedures including routine use of external control materials with each batch of testing and routine evaluation of internal normal epithelial elements or the inclusion of normal breast sections on each tested slide, wherever possible.

Regular, ongoing assay reassessment should be done at least semiannually (as described in Fitzgibbons et al[1]). Revalidation is needed whenever there is a significant change to the test system.

Ongoing competency assessment and education of pathologists.

Optimal external proficiency assessment

Recommendation:

Mandatory participation in external proficiency testing program with at least two testing events (mailings) per year.

Satisfactory performance requires at least 90% correct responses on graded challenges for either test.

Comments:

Unsatisfactory performance will require laboratory to respond according to accreditation agency program requirements.

Optimal laboratory accreditation

Recommendation:

On-site inspection every other year with annual requirement for self-inspection.

Comments:

Reviews laboratory validation, procedures, QA results and processes, and reports.

Unsuccessful performance results in suspension of laboratory testing for ER or PgR.

Abbreviations: ER, estrogen receptor; PgR, progesterone receptor; IHC, immunohistochemistry; QA, quality assurance; NBF, neutral buffered formalin; ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; HER2, human epidermal growth factor receptor 2.

1. Fitzgibbons PL, Murphy DA, Hammond ME, et al. Recommendations for validating estrogen and progesterone receptor immunohistochemistry assays. *Arch Pathol Lab Med.* 2010;134:930–935.