CYP2D6 Genotyping, Tamoxifen and Breast Cancer

Description

Tamoxifen, a selective estrogen receptor modulator (SERM), is the standard of care for premenopausal women with estrogen or progesterone receptor-positive breast cancer and a valid option for treating post-menopausal women. However, a substantial number of tamoxifen-treated patients relapse following surgical resection, while others remain disease-free for many years. Tamoxifen activity is directly related to its active metabolites rather than tamoxifen itself. Cytochrome P450 (CYP) enzymes, CYP2D6 in particular, play a major role in the metabolism of tamoxifen to active metabolites. More than 75 germline CYP2D6 variants have been identified.[1]

Testing for CYP2D6 variants is proposed to predict patients who are likely to fail to respond to tamoxifen. Identifying such patients could supplement information used by clinicians and patients in treatment decision-making. For patients in whom tamoxifen is expected to have little activity, physicians and patients may opt to initiate an alternative therapy.[1]

Tissue tested: Blood specimen
Testing available: Multiple labs, including ARUP and LabCorp

Recommendation: ASCO guidelines (2009),[2] corroborated by an AHRQ-funded systematic review (2010) as well as more recent reports, state that CYP2D6 genotyping is **not** useful in guiding choices about the use of adjuvant tamoxifen in women with hormone-positive breast cancer.

- Emerging evidence suggests that more comprehensive genotyping of the CYP2D6 gene (i.e., more alleles), perhaps in combination with genotyping of additional genes involved in tamoxifen metabolism, shows promise in providing useful predictive value for tamoxifen use.
- Many experts continue to suggest that for women taking tamoxifen, irrespective of CYP2D6 gene status, avoidance of strong CYP2D6-inhibiting drugs (e.g., paroxetine) is prudent.

Key References

1. Dahabreh I, Terasawa T, Castaldi P, Trikalinos TA. CYP2D6 testing to predict response to tamoxifen in women with breast cancer. Pharmacogenomic. PLoS Curr 2010;2.
2. Visvanathan K, Chlebowski RT, Hurley P, et al. American society of clinical oncology clinical practice guideline update on the use of pharmacologic interventions including tamoxifen, raloxifene, and aromatase inhibition for breast cancer risk reduction. J Clin Oncol 2009;27:3235-58.
3. Tufts's EPC for AHRQ. *Systematic Reviews on Selected Pharmacogenetic Tests for Cancer Treatment: CYP2D6 for Tamoxifen in Breast Cancer, KRAS for anti-EGFR antibodies in Colorectal Cancer, and BCR-ABL1 for Tyrosine Kinase Inhibitors in Chronic Myeloid Leukemia*. June 7, 2010.

Centers for Medicare and Medicaid Services:
http://www.cms.gov/mcd/viewtechassess.asp?from2=viewtechassess.asp&where=index&tid=76&